```
=> d his full
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 L_2

(FILE 'HOME' ENTERED AT 08:18:34 ON 17 OCT 2005)

FILE 'HCAPLUS' ENTERED AT 08:19:26 ON 17 OCT 2005 2 SEA ABB=ON PLU=ON (US2003158101 OR US5990077)/PN OR (US2002-0 L142746# OR US96-632533# OR US95-422540#)/AP,PRN

FILE 'REGISTRY' ENTERED AT 08:19:53 ON 17 OCT 2005

FILE 'HCAPLUS' ENTERED AT 08:19:53 ON 17 OCT 2005 TRA L1 1- RN : 14 TERMS

FILE 'REGISTRY' ENTERED AT 08:19:54 ON 17 OCT 2005 L3 14 SEA ABB=ON PLU=ON L2

FILE 'WPIX' ENTERED AT 08:19:56 ON 17 OCT 2005 5 SEA ABB=ON PLU=ON (US2003158101 OR US5990077)/PN OR (US2002-0 L4 42746# OR US96-632533# OR US95-422540#)/AP,PRN

FILE 'REGISTRY' ENTERED AT 08:20:11 ON 17 OCT 2005 D SAV ACT HAR746C1/A

47 SEA ABB=ON PLU=ON (GLUCAGON (W) (RELATED OR LIKE) (W) PEPTIDE L5 (W) II) / CNS

ACT HAR746C2/A

45) SEA ABB=ON PLU=ON [HRK] HADGSFSDEMNTILDNLA [ASTPG] RDFINWLIQTKIT L6 D/SOSP

87) SEA ABB=ON PLU=ON HADGSFSDEMNTILDNLA [ASTPG] RDFINWLIQTKITD/SQS 1.7 P

87 SEA ABB=ON PLU=ON (L6 OR L7) L8 -----

FILE 'HCAPLUS' ENTERED AT 08:20:39 ON 17 OCT 2005

ACT HAR746T1/A _ _ _ _ _ _ _ _ _

103 SEA ABB=ON PLU=ON (GLUCAGON (W) (RELATED OR LIKE) (W) PEPTIDE L9 OR GLP) (W) II OR GLPII

375 SEA ABB=ON PLU=ON L5 L10

382 SEA ABB=ON PLU=ON (L9 OR L10) 93 SEA ABB=ON PLU=ON L8 L11

L12 E GASTROINTESTINAL/CT

E E9+ALL

E E2

E E3+ALL

QUE ABB=ON PLU=ON DIGESTIVE TRACT, DISEASE+OLD, NT/CT T₁13

E E597

E E3+ALL

QUE ABB=ON PLU=ON DIGESTIVE TRACT+NT/CT L14

E E84+ALL

4298 SEA ABB=ON PLU=ON DIGESTION, BIOLOGICAL+OLD, NT/CT L15 L16

QUE ABB=ON PLU=ON PY<=1996 OR AY<=1996 OR PRY<=1996 OR

PD<=19960412 OR AD<=19960412 OR PRD<=19960412

251 SEA ABB=ON PLU=ON L11 AND (L13 OR L14 OR L15) L17

E DRUCKER D/AU

287 SEA ABB=ON PLU=ON ("DRUCKER D"/AU OR "DRUCKER D B"/AU OR L18 "DRUCKER D C"/AU OR "DRUCKER D J"/AU OR "DRUCKER DANIEL"/AU OR "DRUCKER DANIEL C"/AU OR "DRUCKER DANIEL CHARLES"/AU OR "DRUCKER DANIEL J"/AU)

E 1149336/CS, PA

12 SEA ABB=ON PLU=ON (1149336/CS OR 1149336/PA OR "1149336 L19 ONTARIO INC"/CS OR "1149336 ONTARIO INC"/PA OR "1149336

```
ONTARIO INC CAN"/CS OR "1149336 ONTARIO INC CAN"/PA)
            49 SEA ABB=ON PLU=ON L17 AND (L18 OR L19)
L20
L21
            19 SEA ABB=ON PLU=ON L20 AND L13
          108 SEA ABB=ON PLU=ON L11 (L)THU/RL
L22
            14 SEA ABB=ON PLU=ON L22 AND L21 202 SEA ABB=ON PLU=ON L17 NOT L20
L23
L24
             35 SEA ABB=ON PLU=ON L24 AND L16
L25
              5 SEA ABB=ON PLU=ON L25 AND L22
L26
                E ABSORPTION/CT
                E E3+ALL
                E ABSORPTION/CT
                E E4+ALL
                E E2
                E E3+ALL
                E BIOLOGICAL TRANSPORT/CT
                E E3+ALL
L27
          58906 SEA ABB=ON PLU=ON BIOLOGICAL TRANSPORT+NT/CT (L) (UPTAK? OR
                ABSORP?)
                E SMALL INTESTINE/CT
                E E3+AL
                E E3+ALL
                E E2+ALL
                E INTESTINE/CT
                E E3+ALL
L28
         142558 SEA ABB=ON PLU=ON INTESTINE+OLD, NT/CT
           2886 SEA ABB=ON PLU=ON L27 AND (SMALL (1A)INTESTIN? OR JEJUN? OR
L29
                DUODEN? OR ILE?)
            576 SEA ABB=ON PLU=ON L27 (L) (SMALL (1A)INTESTIN? OR JEJUN? OR
L30
                DUODEN? OR ILE?)
              O SEA ABB=ON PLU=ON (L29 OR L30) AND L12
L31
L32
             32 SEA ABB=ON PLU=ON L28 AND L12
L33
              O SEA ABB=ON PLU=ON L32 AND L27
             5 SEA ABB=ON PLU=ON L32 AND ?ABSORP?
L34
                            PLU=ON
                                   L12 AND (L17 OR L18)
L35
             48 SEA ABB=ON
             32 SEA ABB=ON PLU=ON L12 AND (L27 OR L28)
L36
             5 SEA ABB=ON PLU=ON L36 AND ?ABSORP?
L37
L38
              O SEA ABB=ON PLU=ON L37 NOT L34
              5 SEA ABB=ON PLU=ON (L34 OR L37)
1.39
     FILE 'MEDLINE' ENTERED AT 09:16:01 ON 17 OCT 2005
             12 SEA ABB=ON PLU=ON (L9 OR L10)
L40
              O SEA ABB=ON PLU=ON L8
L41
                E GLUCAGOC/CT
                E GLUCAGON/CT
                E E3+ALL
                E GLUCAGON-LIKE/CT
                E GLUCAGON LIKE/CT
                E GLP/CT
     FILE 'EMBASE' ENTERED AT 09:18:28 ON 17 OCT 2005
L42
             15 SEA ABB=ON PLU=ON (L9 OR L10)
              O SEA ABB=ON PLU=ON L8
L43
              3 SEA ABB=ON PLU=ON (2005124077/AN OR 2005369960/AN OR
L44
                2005384300/AN) AND L42
     FILE 'BIOSIS' ENTERED AT 09:20:54 ON 17 OCT 2005
            290 SEA ABB=ON PLU=ON (L9 OR L10)
L45
              O SEA ABB=ON PLU=ON L8
T.46
                E STOMACH DISAESE/CT
                E GASTROINTEST/CT
                E GASTROINTESTINAL DIS/CT
L47
           3382 SEA ABB=ON PLU=ON GASTROINTESTINAL DISEASE#
              4 SEA ABB=ON PLU=ON L47 AND L45
L48
L49
              3 SEA ABB=ON PLU=ON ("2003:106962"/AN OR "2004:42129"/AN OR
                "2005:59078"/AN) AND L48
```

FILE 'HCAPLUS' ENTERED AT 09:24:01 ON 17 OCT 2005 L50 16 SEA ABB=ON PLU=ON (L23 OR L39)

=> b reg

FILE 'REGISTRY' ENTERED AT 09:25:15 ON 17 OCT 2005

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STRUCTURE FILE UPDATES: 16 OCT 2005 HIGHEST RN 865349-47-9 DICTIONARY FILE UPDATES: 16 OCT 2005 HIGHEST RN 865349-47-9

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d que sta 15

L5 47 SEA FILE=REGISTRY ABB=ON PLU=ON (GLUCAGON (W) (RELATED OR LIKE) (W) PEPTIDE (W) II)/CNS

=> d que sta 18

L6 (45)SEA FILE=REGISTRY ABB=ON PLU=ON [HRK]HADGSFSDEMNTILDNLA [ASTPG]RDFINWLIQTKITD/SQSP

L7 (87)SEA FILE=REGISTRY ABB=ON PLU=ON HADGSFSDEMNTILDNLA [ASTPG] RDFI NWLIQTKITD/SQSP

L8 87 SEA FILE=REGISTRY ABB=ON PLU=ON (L6 OR L7)

=> b hcap FILE 'HCAPLUS' ENTERED AT 09:25:26 ON 17 OCT 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 17 Oct 2005 VOL 143 ISS 17 FILE LAST UPDATED: 16 Oct 2005 (20051016/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all fhitstr 150 tot

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L50 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
     2004:817916 HCAPLUS
AN
DN
     141:326195
    Entered STN: 07 Oct 2004
ED
    Synthesis of protracted GLP-2 derivatives attached to an hydrophilic
ΤI
     substituent and therapeutic uses thereof
    Kodra, Janos Tibor; Johansen, Nils Langeland; Thim, Lars; Peschke, Bernd
TN
PΑ
    Novo Nordisk A/S, Den.
     PCT Int. Appl., 66 pp.
SO
```

- CODEN: PIXXD2 DTPatent
- LΑ English
- IC ICM C07K014-605
 - ICS A61K038-26; A61P001-00; A61K047-48

P

- 2-6 (Mammalian Hormones)
 - Section cross-reference(s): 34, 63

FAN.CNT 1

	PATENT NO.				KIND		DATE		APPLICATION NO.						DATE			
							-											
ΡI	WO 2004085471				A2 2004100		1007	WO 2004-DK198						20040323				
	WO	2004	04085471				A3 20041104											
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NΑ,	NΙ,
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
			ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	zw
		RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	ŪĠ,	ZM,	ZW,	AM,	ΑZ,
			BY,	KG,	ΚZ,	MD,	RU,	TJ,	TM,	AT,	BE,	ВG,	CH,	CY,	CZ,	DE,	DK,	EE,
			ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,
			SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,
			TD,	TG														
PRAI	DK	2003	-451			Α		2003	0324									

US 2003-459838P

PATENT NO.	 PATENT FAMILY CLASSIFICATION CODES
WO 2004085471	
WO 2004085471	 A61K047/48H4P; C07K014/605

20030402

- OS MARPAT 141:326195
- AB The present invention relates to novel derivs. of human glucagon-like peptide-2 (GLP-2) peptides which have a protracted profile of action, as well as pharmaceutical compns., uses and methods of treatment.
- ST GLP2 deriv hydrophilic substituent synthesis intestine nutrient malabsorption treatment
- IT Helicobacter pylori
 - (-induced gastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Chemotherapy Radiotherapy

(-induced intestinal damage; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Inflammation (Crohn's disease; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) TT Intestine, disease (Crohn's; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Wound healing (after surgery; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Appetite (anorexia nervosa; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Carbohydrates, reactions RL: RCT (Reactant); RACT (Reactant or reagent) (as a hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) TΤ Inflammation Stomach, disease (atrophic gastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) TT Intestine, disease (atrophy; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Inflammation Intestine, disease (colitis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) TΤ Carboxylic acids, biological studies RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses) (dicarboxylic, unbranched α, ω , as a spacer between GLP-2 derivative and hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) Inflammation Intestine, disease (enteritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) TΤ Inflammation Stomach, disease (qastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Transplant and Transplantation (graft-vs.-host reaction; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Surgery (healing after; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Hydrophilicity (hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Intestine, disease (injury; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Injury (intestinal; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) ITIntestine, disease (irritable bowel syndrome; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) IT Intestine, disease (malabsorption; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) ITLymphatic system, disease

```
(obstruction; synthesis of protracted GLP-2 derivs. attached to an
        hydrophilic substituent and therapeutic uses thereof)
TT
     Newborn
        (premature; synthesis of protracted GLP-2 derivs. attached to an
        hydrophilic substituent and therapeutic uses thereof)
     Connective tissue, disease
        (scleroderma; synthesis of protracted GLP-2 derivs. attached to an
        hydrophilic substituent and therapeutic uses thereof)
IT
     Intestine, disease
        (short bowel syndrome; synthesis of protracted GLP-2 derivs. attached
        to an hydrophilic substituent and therapeutic uses thereof)
TT
     Antidiarrheals
     Antiulcer agents
     Bacteremia
     Blood vessel, disease
     Dehydration, physiological
     Drug delivery systems
     Osteoporosis
     Protein sequences
     Sepsis
     Ulcer
        (synthesis of protracted GLP-2 derivs. attached to an hydrophilic
        substituent and therapeutic uses thereof)
TT
    Diarrhea
        (tourist; synthesis of protracted GLP-2 derivs. attached to an
        hydrophilic substituent and therapeutic uses thereof)
IT
     Celiac disease
        (tropical and non-tropical; synthesis of protracted GLP-2 derivs.
        attached to an hydrophilic substituent and therapeutic uses thereof)
                                                 768850-01-7DP,
TТ
     768850-00-6DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
                                  768850-02-8DP, polyalkyleneglycol derivs.
     768850-03-9DP, polyalkyleneglycol derivs.
                                                  768850-04-0DP,
                                  768850-05-1DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-06-2DP, polyalkyleneglycol derivs.
                                                  768850-07-3DP
     polyalkyleneglycol derivs.
                                  768850-08-4DP, polyalkyleneglycol derivs.
     768850-09-5DP, polyalkyleneglycol derivs.
                                                  768850-10-8DP,
     polyalkyleneglycol derivs.
                                   768850-11-9DP, polyalkyleneglycol derivs.
     768850-12-0DP, polyalkyleneglycol derivs.
                                                  768850-13-1DP
     polyalkyleneglycol derivs.
                                   768850-14-2DP, polyalkyleneglycol derivs.
     768850-15-3DP, polyalkyleneglycol derivs.
                                                  768850-17-5DP
                                   768850-18-6DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-19-7DP, polyalkyleneglycol derivs.
                                                  768850-20-0DP,
     polyalkyleneglycol derivs.
                                   768850-21-1DP, polyalkyleneglycol derivs.
     768850-22-2DP, polyalkyleneglycol derivs.
                                                  768850-23-3DP,
                                   768850-24-4DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-25-5DP, polyalkyleneglycol derivs.
                                                  768850-26-6DP,
     polyalkyleneglycol derivs.
                                  768850-27-7DP, polyalkyleneglycol derivs.
     768850-28-8DP, polyalkyleneglycol derivs.
                                                  768850-29-9DP,
                                   768850-30-2DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-31-3DP, polyalkyleneglycol derivs.
                                                  768850-32-4DP
     polyalkyleneglycol derivs.
                                   768850-35-7DP, polyalkyleneglycol derivs.
     768850-36-8DP, polyalkyleneglycol derivs.
                                                  768850-37-9DP,
     polyalkyleneglycol derivs.
                                   768850-38-0DP, polyalkyleneglycol derivs.
     768850-39-1DP, polyalkyleneglycol derivs.
                                                  768850-40-4DP,
                                   768850-41-5DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
     768850-42-6DP, polyalkyleneglycol derivs.
                                                  768850-43-7DP
     polyalkyleneglycol derivs.
                                   768850-44-8DP, polyalkyleneglycol derivs.
                                                  768850-46-0DP,
     768850-45-9DP, polyalkyleneglycol derivs.
                                   768850-47-1DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
                                                  768850-49-3DP,
     768850-48-2DP, polyalkyleneglycol derivs.
     polyalkyleneglycol derivs.
                                   768850-50-6DP, polyalkyleneglycol derivs.
                    770731-78-7P
                                   770731-79-8P
     770731-77-6P
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
```

```
(amino acid sequence; synthesis of protracted GLP-2 derivs. attached to
        an hydrophilic substituent and therapeutic uses thereof)
IT
     223460-79-5, 1-33-Glucagon-like peptide II (human)
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to
        an hydrophilic substituent and therapeutic uses thereof)
                                                             768850-02-8
IT
     197922-42-2
                  197922-46-6
                                768850-00-6
                                               768850-01-7
     768850-03-9
                   768850-04-0
                                 768850-05-1
                                               768850-06-2
                                                             768850-07-3
                   768850-09-5
                                                             768850-12-0
     768850-08-4
                                 768850-10-8
                                               768850-11-9
     768850-13-1
                   768850-14-2
                                 768850-15-3
                                               768850-16-4
                                                             768850-17-5
                                                             768850-22-2
     768850-18-6
                   768850-19-7
                                 768850-20-0
                                               768850-21-1
                                               768850-26-6
                                                             768850-27-7
     768850-23-3
                   768850-24-4
                                 768850-25-5
                                               768850-31-3
                                 768850-30-2
     768850-28-8
                   768850-29-9
                                                             768850-32-4
                                                             768850-37-9
     768850-33-5
                   768850-34-6
                                 768850-35-7
                                               768850-36-8
                   768850-39-1
                                 768850-40-4
                                               768850-41-5
                                                             768850-42-6
     768850-38-0
                   768850-44-8
                                 768850-45-9
                                               768850-46-0
                                                             768850-47-1
     768850-43-7
     768850-48-2
                   768850-49-3
                                 768850-50-6
     RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
        (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to
        an hydrophilic substituent and therapeutic uses thereof)
IT
     7512-17-6, 2-Acetamido-2-deoxy-D-glucose
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (as a hydrophilic substituent; synthesis of protracted GLP-2 derivs.
        attached to an hydrophilic substituent and therapeutic uses thereof)
     56-12-2, \gamma-Aminobutyric acid, biological studies
                                                        56-84-8,
IT
     L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological
     studies
              56-87-1, L-Lysine, biological studies 107-95-9, β-Alanine
     RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological
     study); RACT (Reactant or reagent); USES (Uses)
        (as a spacer between GLP-2 derivative and hydrophilic substituent;
        synthesis of protracted GLP-2 derivs. attached to an hydrophilic
        substituent and therapeutic uses thereof)
     89750-15-2DP, Glucagon-like peptide-2, derivs.
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (synthesis of protracted GLP-2 derivs. attached to an hydrophilic
        substituent and therapeutic uses thereof)
     89750-15-2, Glucagon-like peptide-2
IT
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (synthesis of protracted GLP-2 derivs. attached to an hydrophilic
        substituent and therapeutic uses thereof)
IT
     20866-46-0 35661-39-3
                              35661-40-6
                                            35661-60-0
                                                         71989-14-5
     71989-18-9
                  71989-23-6
                               71989-28-1
                                            71989-33-8
                                                         71989-35-0
                                 132327-80-1
                  131287-39-3
                                               132388-59-1
                                                            143824-78-6
     119831-72-0
     148515-84-8
                  150629-67-7
                                 174569-25-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (synthesis of protracted GLP-2 derivs. attached to an hydrophilic
        substituent and therapeutic uses thereof)
TΤ
     223460-79-5, 1-33-Glucagon-like peptide II (human)
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to
        an hydrophilic substituent and therapeutic uses thereof)
     223460-79-5 HCAPLUS
RN
     1-33-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
L50
AN
     2004:592387 HCAPLUS
DN
     141:167958
     Entered STN: 26 Jul 2004
ED
     GLP-2 (glucagon-like peptide-2) controls energy homeostasis by
TI
```

```
proliferative and cytoprotection actions in the gastrointestinal
     epithelium
ΑU
     Yusta, B.; Drucker, D. J.
     Departement de Medecine, Hopital General de Toronto, Centre du diabete
CS
     Banting et Best, Universite de Toronto, Toronto, ON, M5G 2C4, Can.
     Journees Annuelles de Diabetologie de l'Hotel-Dieu (2004) 127-137
SO
     CODEN: JDBHAC; ISSN: 0075-4439
PB
     Flammarion Medecine-Sciences
DT
     Journal; General Review
     French
LΑ
CC
     2-0 (Mammalian Hormones)
     A review. The proliferative and cytoprotective effects of glucagon-like
AB
     peptide-2 (GLP-2) on the gastrointestinal epithelium are review here, with
     particular emphasis on the anti-apoptotic signaling pathway of GLP-2
     receptor and the potential therapeutic applications of GLP-2 from its
     action on various exptl. intestinal disorders.
     review glucagon like peptide gastrointestinal epithelium proliferation
ST
     cytoprotection metab
TΤ
     Cell proliferation
       Digestive tract, disease
     Energy metabolism, animal
        (GLP-2 (glucagon-like peptide-2) controls energy homeostasis by
        proliferative and cytoprotection actions in gastrointestinal
        epithelium)
IT
     Cytoprotective agents
         (GLP-2 as; GLP-2 (glucagon-like peptide-2) controls energy homeostasis
        by proliferative and cytoprotection actions in gastrointestinal
        epithelium)
     Epithelium
IT
         (digestive tract; GLP-2 (glucagon-like peptide-2) controls energy
        homeostasis by proliferative and cytoprotection actions in
        gastrointestinal epithelium)
IT
     Digestive tract
         (epithelium; GLP-2 (glucagon-like peptide-2) controls energy
        homeostasis by proliferative and cytoprotection actions in
        gastrointestinal epithelium)
     89750-15-2, Glucagon-like peptide-2
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (GLP-2 (glucagon-like peptide-2) controls energy homeostasis by
        proliferative and cytoprotection actions in gastrointestinal
        epithelium)
RE.CNT
              THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
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Entered STN: 30 Apr 2004
ED
     Synthesis and production of glucagon-like peptide-2 (GLP-2) derivatives
TΙ
     and, formulations and therapeutic uses thereof
IN
     Thim, Lars; Bang, Susanne; Schlein, Morten; Kaarsholm, Niels Christian;
     Engelund, Dorthe Kot; Nielsen, Anette Sams; Johansen, Nils Langeland; Madsen, Kjeld; Zundel, Magali; Thygesen, Peter
     Novo Nordisk A/S, Den.
PΑ
     PCT Int. Appl., 195 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
     ICM C07K014-605
IC
     2-6 (Mammalian Hormones)
CC
     Section cross-reference(s): 16, 34
FAN.CNT 1
     PATENT NO.
                          KIND
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                                              WO 2003-DK694
PΙ
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                                 20040429
                                                                       20031014
     WO 2004035624
                          A3
                                 20040910
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                                                                      20031014
     EP 1554308
                          A2
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                 20050802
                                            BR 2003-14920
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PRAI DK 2002-1574
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     US 2002-420581P
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                                 20021114
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     US 2002-434562P
                          P
                                20021219
     WO 2003-DK694
                           W
                                 20031014
CLASS
                 CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
                 ____
 WO 2004035624 ICM C07K014-605
 WO 2004035624 ECLA C07K014/605
 US 2004122210
                NCL
                         530/324.000
                  ECLA
                        C07K014/605
     MARPAT 140:386446
os
     The present invention relates to novel human glucagon-like peptide-2
AΒ
     (GLP-2) peptides and human glucagon-like peptide-2 derivs. which have a
     protracted profile of action as well as polynucleotide constructs encoding
     such peptides, vectors and host cells comprising and expressing the
     polynucleotide, pharmaceutical compns., uses and methods of treatment.
     GLP2 deriv synthesis intestine bone treatment formulation fermn prodn
ST
TT
     Helicobacter pylori
         (-induced gastritis; synthesis and production of glucagon-like peptide-2
         (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
     Chemotherapy
         (-induced tissue injury; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
ΙT
     Immobilization, animal
         (-related bone loss; synthesis and production of glucagon-like peptide-2
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(GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
    Rheumatoid arthritis
        (-related periarticular erosions; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
     Parkinson's disease
IT
        (-related weight loss; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
        (Crohn's disease; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
     Intestine, disease
        (Crohn's; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
     Fatty acids, reactions
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (C12; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
     Fatty acids, reactions
TТ
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (C16; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs.
        and, formulations and therapeutic uses thereof)
IT
     Brain
     Heart
     Kidney
     Liver
     Lung
     Muscle
     Spleen
     Stomach
        (GLP-2 receptor expression level in; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Bone, disease
        (Paget's; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     Solid phase synthesis supports
        (Wang resins; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
TΤ
     Wound healing
        (after surgery; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     Drugs
        (appetite stimulants; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
     Disease, animal
        (arthropathy, erosion, rheumatoid arthritis-related; synthesis and
        production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
     Peptides, reactions
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (as a spacer linking GLP-2 derivative to a lipophilic substituent;
        synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
        formulations and therapeutic uses thereof)
IT
     Inflammation
     Stomach, disease
         (atrophic gastritis; synthesis and production of glucagon-like peptide-2
         (GLP-2) derivs. and, formulations and therapeutic uses thereof)
ΤТ
     Muscle, disease
        (atrophy, post-radiation; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
IT
     Injury
         (bone; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs.
        and, formulations and therapeutic uses thereof)
IT
     Inflammation
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Intestine, disease
        (colitis; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     Intestine
        (colon, GLP-2 receptor expression level in; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Joint, anatomical
        (disease, erosion, rheumatoid arthritis-related; synthesis and production
        of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
TT
     Intestine
        (duodenum, GLP-2 receptor expression level in; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Inflammation
       Intestine, disease
        (enteritis; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
     Intestine, disease
        (failure; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     Genetic vectors
        (for GLP-2 analogs production; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
     Inflammation
TT
     Stomach, disease
        (gastritis; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     G protein-coupled receptors
     Hormone receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (glucagon-like peptide-2, localization; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Transplant and Transplantation
        (graft-vs.-host reaction; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
TT
     Bos taurus
     Cavia porcellus
     Gallus domesticus
     Mesocricetus auratus
     Octodon degus
     Rattus
     Salamander
     Sus scrofa domestica
        (human GLP-2 sequence compared to that of; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Intestine
        (ileum, GLP-2 receptor expression level in; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
ΙT
     Species differences
        (in GLP-2 sequence; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
        (infectious; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
ΙT
     Intestine, disease
        (inflammatory; synthesis and production of glucagon-like peptide-2 (GLP-2)
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derivs. and, formulations and therapeutic uses thereof)
IT
     Bone, disease
       Intestine, disease
        (injury; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
TT
        (intestinal mucosal; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
IT
     Injury
        (intestinal; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
TT
     Intestine
        (jejunum, GLP-2 receptor expression level in; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Lipophilicity
        (lipophilic substituent attached to GLP-2 derivs.; synthesis and production
        of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Body weight
        (loss, Parkinson's disease-related; synthesis and production of
        qlucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Intestine, disease
        (malabsorption; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
IT
     Bone, neoplasm
        (metastasis; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IТ
     Intestine, disease
        (mucosal injury; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
     Lymphatic system, disease
IT
        (obstruction; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
ΙT
     Myositis
        (ossificans; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     Bone, disease
        (osteodystrophy; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
TТ
     Bone, disease
        (osteopenia; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     Bone, disease
        (osteopetrosis; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
IT
     Inflammation
     Pancreas, disease
        (pancreatitis; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
TТ
     Nutrition, animal
        (parenteral, total, -induced intestinal atrophy; synthesis and production
        of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Newborn
        (premature, intestinal failure in; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Fermentation
        (production of GLP-2 analogs by; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
TΤ
     Saccharomyces cerevisiae
     Yeast
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(production of GLP-2 analogs in; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
TΤ
    Bone
        (resorption, inhibitors; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
IT
     Bone
        (resorption; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
TT
     Connective tissue, disease
        (scleroderma; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
TT
     Protein degradation
        (sensitivity of GLP-2 analogs to; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
     Shock (circulatory collapse)
IT
        (septic, -related ulcers; synthesis and production of glucagon-like
        peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
        thereof)
IT
     Steroids, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (sex, deficiency-related bone loss; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
     Intestine, disease
TT
        (short bowel syndrome; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
тт
     Inflammation
     Spinal column, disease
        (spondylitis, Bechterew's disease; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
IT
     Sex hormones
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (steroidal, deficiency-related bone loss; synthesis and production of
        glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
        therapeutic uses thereof)
        (stimulants; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
ΙT
     Anorexia
    Antidiarrheals
     Antitumor agents
     Antiulcer agents
     Bacteremia
     Blood vessel, disease
     Bone, neoplasm
     Celiac disease
     Dehydration, physiological
     Diarrhea
     Drug delivery systems
     Gastrointestinal agents
    Human
     Hyperparathyroidism
     Osteomalacia
     Osteoporosis
     Periodontium, disease
     Protein sequences
     Sepsis
     Wound healing promoters
        (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
        formulations and therapeutic uses thereof)
IT
     Fatty acids, reactions
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RL: RCT (Reactant); RACT (Reactant or reagent)
        (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
        formulations and therapeutic uses thereof)
IT
     Inflammation
       Intestine, disease
        (ulcerative colitis; synthesis and production of glucagon-like peptide-2
        (GLP-2) derivs. and, formulations and therapeutic uses thereof)
     223460-79-5, 1-33-Glucagon-like peptide II (human)
IT
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (amino acid sequence; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
     56-12-2, γ-Aminobutyric acid, reactions 56-84-8, L-Aspartic acid,
TT
                 56-86-0, L-Glutamic acid, reactions 56-87-1, L-Lysine,
     reactions
     reactions
                 107-95-9, β-Alanine
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (as a spacer linking GLP-2 derivative to a lipophilic substituent;
        synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
        formulations and therapeutic uses thereof)
     7440-70-2, Calcium, biological studies
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (hypercalcemia; synthesis and production of glucagon-like peptide-2 (GLP-2)
        derivs. and, formulations and therapeutic uses thereof)
     89750-15-2DP, Glucagon-like peptide II, analogs 682841-20-9P
IT
                    682841-22-1P
                                    682841-23-2P
                                                    682841-24-3P
                                                                    682841-25-4P
     682841-21-0P
     682841-26-5P
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                                    682841-28-7P
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     PREP (Preparation); USES (Uses)
        (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
        formulations and therapeutic uses thereof)
IT
     89750-15-2, Glucagon-like peptide II
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
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TT
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     35661-60-0
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        (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and,
        formulations and therapeutic uses thereof)
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     223460-79-5, 1-33-Glucagon-like peptide II (human)
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     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
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        (amino acid sequence; synthesis and production of glucagon-like peptide-2
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L50
     2002:657973 HCAPLUS
AN
DN
     137:190756
ED
     Entered STN: 30 Aug 2002
     Enhancement of GLP-2 activity for treatment of gastrointestinal disorders
TI
     and suppression of appetite
     Drucker, Daniel J.; Lovshin, Julie Ann Louise
IN
PΑ
     Can.
so
     PCT Int. Appl., 32 pp.
     CODEN: PIXXD2
DT
     Patent
LА
     English
     ICM A61K045-00
IC
     63-6 (Pharmaceuticals)
CC
     Section cross-reference(s): 1
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                 NCL
                        514/008.000
                       A61K038/26; A61K038/26+M; A61K045/06
                 ECLA
     The effects of GLP-2 (glucagon-like peptide-2) are enhanced using a GLP-1
AB
     activity inhibitor. For medical use to treat or inhibit the onset of
     medical conditions, disorder or diseases for which treatment with GPL-2 is
     indicated, the present invention provides a pharmaceutical combination
     comprising a GLP-2 activity enhancer, and a GLP-1 activity inhibitor. The
     combination is useful particularly to treat gastrointestinal conditions
     such as small bowel syndrome, mucositis and Crohn's disease, and to
     suppress appetite, for instance to treat obesity.
     GLP2 enhancement antiobesity appetite depressant gastrointestinal disease
ST
IT
     Inflammation
        (Crohn's disease; enhancement of GLP-2 activity for treatment of
        gastrointestinal disorders and suppression of appetite)
IT
     Intestine, disease
        (Crohn's; enhancement of GLP-2 activity for treatment of
        gastrointestinal disorders and suppression of appetite)
TT
    Mucous membrane
        (disease, inflammation; enhancement of GLP-2 activity for treatment of
        gastrointestinal disorders and suppression of appetite)
IT
     Antiobesity agents
    Appetite depressants
       Digestive tract, disease
     Drug delivery systems
     Human
     Obesity
        (enhancement of GLP-2 activity for treatment of gastrointestinal
        disorders and suppression of appetite)
     G protein-coupled receptors
IT
     Hormone receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (glucagon-like peptide-2, agonists; enhancement of GLP-2 activity for
        treatment of gastrointestinal disorders and suppression of appetite)
IT
     Intestine, disease
        (irritable bowel syndrome; enhancement of
        GLP-2 activity for treatment of gastrointestinal disorders and
        suppression of appetite)
IT
     Inflammation
        (mucous membrane; enhancement of GLP-2 activity for treatment of
        gastrointestinal disorders and suppression of appetite)
IT
     213190-65-9, Exendin
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (enhancement of GLP-2 activity for treatment of gastrointestinal
        disorders and suppression of appetite)
     89750-15-2, Glucagon-like peptide 2
TT
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (enhancers; enhancement of GLP-2 activity for treatment of
        gastrointestinal disorders and suppression of appetite)
IT
     89750-14-1, Glucagon-like peptide I
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RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors; enhancement of GLP-2 activity for treatment of
        gastrointestinal disorders and suppression of appetite)
IT
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     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (enhancers; enhancement of GLP-2 activity for treatment of
        gastrointestinal disorders and suppression of appetite)
RN
     89750-15-2 HCAPLUS
    Glucagon-like peptide II (9CI) (CA INDEX NAME)
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
L50 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
    2002:213328 HCAPLUS
DN
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     Entered STN: 21 Mar 2002
ED
    Gut adaptation and the glucagon-like peptides
TТ
ΑIJ
    Drucker, D. J.
    The Banting and Best Diabetes Centre, University of Toronto, Toronto, ON,
CS
    M5G 2C4, Can.
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    Gut (2002), 50(3), 428-435
    CODEN: GUTTAK; ISSN: 0017-5749
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    BMJ Publishing Group
DT
    Journal; General Review
    English
LΑ
CC
    2-0 (Mammalian Hormones)
    A review. The glucagon-like peptides are synthesized in and released from
AB
     enteroendocrine cells in the small and large intestine. Glucagon-like
     peptide 1 (GLP-1) promotes efficient nutrient assimilation via effects on
     food intake, gastric emptying, stimulation of insulin secretion, and
     control of islet proliferation. Glucagon-like peptide 2 (GLP-2), a 33
     amino acid peptide cosecreted with GLP-1, regulates energy absorption via
     effects on nutrient intake, gastric acid secretion and gastric emptying,
     nutrient absorption, and mucosal permeability. GLP-2 secretion is
     stimulated by nutrients, and plasma levels of circulating GLP-2 are
     elevated in the setting of intestinal injury. GLP-2 is enzymically
     inactivated by dipeptidyl peptidase IV by cleavage at the position 2
     alanine, hence the native peptide has a t1/2 of minutes in vivo.
     Exogenous administration of GLP-2 promotes expansion of the mucosal
     epithelium via stimulation of crypt cell proliferation and inhibition of
     crypt and enterocyte apoptosis, leading to an increase in mucosal surface
     area. Administration of GLP-2 in the setting of exptl. intestinal injury
     reduces the extent of mucosal damage in both the small and large
     intestine. GLP-2 augments the endogenous adaptive response to small bowel
     resection and stimulates nutrient absorption in the normal and injured
    mucosal epithelium. The actions of GLP-2 are mediated by a recently
     identified G protein coupled receptor expressed in endocrine cells and
     enteric neurons of the stomach, small bowel, and colon. Preliminary human
     studies demonstrate that GLP-2 may enhance energy absorption and reduce
     fluid loss in subjects with short bowel syndrome. The available evidence
     suggests that GLP-2 functions as a key regulator of mucosal integrity,
     permeability, and nutrient absorption and hence GLP-2 may potentially be
     therapeutically useful in diseases characterized by injury or dysfunction
     of the gastrointestinal epithelium.
ST
     review gut adaptation glucagonlike peptide
IT
     Digestive tract
    Human
       Intestine
       Stomach
        (gut adaptation and glucagon-like peptides)
TТ
     Intestine, disease
        (injury; gut adaptation and glucagon-like peptides)
IT
        (intestinal; gut adaptation and glucagon-like peptides)
TT
     55963-74-1D, Proglucagon, derivs.
                                         89750-14-1, Glucagon-like peptide I
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Page 19

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RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (gut adaptation and glucagon-like peptides)
     89750-15-2, Glucagon-like peptide 2
TT
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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              THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD
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Section cross-reference(s): 1, 14

FAN.CNT 2

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APPLICATION NO.
                                                                 DATE
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                                           B1 20011002 US 1998-149831 19980908
B1 20030701 US 2000-692238 20001020
A1 20031106 US 2003-419150 20030421
PΙ
    US 6297214
    US 6586399
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PRAI US 1997-850664
    US 1998-149831
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                        A3 20001020
CLASS
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US 6297214
                       A61K038-00
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                       514/012.000; 435/366.000; 530/308.000; 530/324.000
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                NCL
                ECLA A61K038/26
                       514/012.000; 435/366.000; 514/002.000; 530/308.000;
                NCL
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                       530/324.000; 530/344.000
                ECLA A61K038/26
 US 2003207809
               NCL
                       514/012.000
                ECLA
                      A61K038/26
    The invention relates to glucagon-related peptides and their use for the
AB
    prevention or treatment of disorders involving the large intestine. In
    particular, it has now been demonstrated that GLP-2 and peptidic agonists
    of GLP-2 can cause proliferation of the tissue of large intestine. Thus,
    the invention provides methods of proliferating the large intestine in a
     subject in need thereof. Further, the methods of the invention are useful
    to treat or prevent inflammatory conditions of the large intestine,
     including inflammatory bowel diseases. Also claimed are methods for
     identifying other peptides useful in treating inflammatory conditions
     involving the large intestine.
ST
     GLP2 analogs delivery large intestine proliferation inflammation disease
     treatment
    Intestine, disease
ΙT
        (Crohn's; large intestine function enhancement and intestinal
        inflammatory disease treatment using glucagon-like peptide 2
       and GLP-2 analogs)
IT
     Intestine, disease
        (colitis, infectious and drug- or chemical-induced; large
        intestine function enhancement and intestinal inflammatory
        disease treatment using glucagon-like peptide 2 and GLP-2 analogs)
     Intestine, disease
TΤ
        (colitis, ischemic; large intestine function enhancement and
        intestinal inflammatory disease treatment using glucagon-like
       peptide 2 and GLP-2 analogs)
IT
     Intestine, disease
        (diverticulitis; large intestine function enhancement and
        intestinal inflammatory disease treatment using glucagon-like
       peptide 2 and GLP-2 analogs)
    G protein-coupled receptors
IT
     Hormone receptors
     Peptide receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (glucagon-like peptide-2, agonists; large intestine function
        enhancement and intestinal inflammatory disease treatment using
        glucagon-like peptide 2 and GLP-2 analogs)
IT
     Intestine, disease
        (inflammatory; large intestine function enhancement and
        intestinal inflammatory disease treatment using glucagon-like
        peptide 2 and GLP-2 analogs)
     Drug delivery systems
        (injections, s.c.; large intestine function enhancement and intestinal
        inflammatory disease treatment using glucagon-like peptide 2 and GLP-2
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analogs)

Cell proliferation Drug screening

IT

(large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) IT (large; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) TΤ Intestine (mucosa; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) IT Drug delivery systems (oral; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) TT Drug delivery systems (rectal; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) IT Intestine (resection, partial or subtotal large intestine; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) TT Intestine, disease (ulcerative colitis; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) 89750-15-2, glucagon-like peptide 2 89750-15-2D, IT glucagon-like peptide 2, analogs 195262-56-7 197664-29-2 197922-42-2 197922-60-4 197923-49-2 223460-79-5, 1-33-Glucagon-like peptide II (human) RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs) THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT (1) Anon; EP 0612531 A1 1994 HCAPLUS (2) Anon; WO 9632414 1996 HCAPLUS (3) Barragan; American Journal of Physiology, Part 1 1994, V266(3), PE459 HCAPLUS (4) Baumann; US 5009956 1991 HCAPLUS (5) Brubaker; Endocrinology 1991, V128(6), P3175 HCAPLUS (6) Buhl; The Journal of Biological chemistry 1998, V263(18), P8621 (7) Calvo; J Neurochem 1995, V64(1), P299 HCAPLUS (8) Chasin, M; Drugs and Pharmaceutical Sciences 1990, V45 HCAPLUS (9) Cheeseman; "The effect of gastric inhibitory polypeptide and glucagon like peptides on intestinal basolaterial membrane hexose transport", APSracts 3:0071G 1996 (10) Cullis; US 5008050 1991 HCAPLUS (11) Dayhoff; Atlas of Protein Sequence and Structure V5, P96 (12) Drucker; US 5789379 1998 HCAPLUS (13) Drucker; US 5834428 1998 HCAPLUS (14) Drucker; US 5952301 1999 HCAPLUS (15) Drucker; US 5990077 1999 HCAPLUS (16) Drucker; Pancreas 1990, V5(4), P484 MEDLINE (17) Drucker; Proc Natl Acad Sci USA 1996, V93, P7911 HCAPLUS (18) Ehrlich; American Journal of Physiology 1994, PE662 HCAPLUS (19) Evans; US 4311712 1982 HCAPLUS (20) Evans; US 4370349 1983 HCAPLUS (21) George; FEBS Letters 1985, V192(2), P275 HCAPLUS (22) Gersonde; US 4452747 1984 HCAPLUS (23) Haynes; US 4725442 1988 HCAPLUS (24) Hoosein; FEBS Letters 1984, V178(1), P83 HCAPLUS (25) Hunt; US 4529561 1985 HCAPLUS

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(33) Orskov; Diabetologia 1987, V30, P874 MEDLINE
(34) Orskov; Endocrinology 1986, V119(4), P1467 MEDLINE
(35) Orskov; FEBS Letters 1989, V247(2), P193 MEDLINE
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(37) Roberts; US 4921706 1990
(38) Suzuki; US 4016100 1977 HCAPLUS
(39) Uster; US 4944948 1990 HCAPLUS
    89750-15-2, glucagon-like peptide 2
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
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     study); USES (Uses)
        (large intestine function enhancement and intestinal inflammatory
       disease treatment using glucagon-like peptide 2 and GLP-2 analogs)
RN
    89750-15-2 HCAPLUS
    Glucagon-like peptide II (9CI) (CA INDEX NAME)
CN
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L50 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
    2001:91506 HCAPLUS
AN
DN
    134:168296
    Entered STN: 07 Feb 2001
ED
    Intestinotrophic glucagon-like peptide-2 analogs
TI
   Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith, Martin
TN
PΑ
   NPS Allelix Corp., Can.
    U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 631,273, abandoned.
SO
    CODEN: USXXAM
DT
    Patent
    English
T.A
IC
    ICM A61K038-26
    ICS A61K038-17; C07K014-605
INCL 514012000
    63-3 (Pharmaceuticals)
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                             19981110 US 1996-669790
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                       A1 20030828 US 2002-293941
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PRAI US 1995-422540
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                              19970408
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 US 6184201
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530/303.000; 530/308.000; 530/324.000
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                        C07K014/605
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                 NCL
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                        C07K014/605
                        514/012.000; 435/366.000; 435/371.000; 514/002.000;
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                        C07K014/605
                        514/012.000; 435/366.000; 435/371.000; 514/002.000;
US 5834428
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                 ECLA
 US 2003158101
                        514/012.000
                 NCL
                        C07K014/605
                 ECLA
os
     MARPAT 134:168296
     Analogs of glucagon-like peptide 2, a product of glucagon gene expression,
AΒ
     have been identified as intestinal tissue growth factors. Their
     formulation as pharmaceuticals and therapeutic use in treating disorders
     of the small bowel are described.
ST
     glucagon like peptide 2 analog intestine therapy sequence
     Intestine, disease
IT
        (Crohn's; intestinotrophic glucagon-like peptide-2 analogs)
TΤ
     Drug delivery systems
        (carriers; intestinotrophic glucagon-like peptide-2 analogs)
     Digestive tract
        (disease; intestinotrophic glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (enteritis; intestinotrophic glucagon-like peptide-2 analogs)
IT
     Digestive tract
        (indigestion; intestinotrophic glucagon-like peptide-2
        analogs)
IT
     Intestine, disease
        (inflammatory; intestinotrophic glucagon-like peptide-2
        analogs)
IT
     Chemotherapy
        (intestinal damage from; intestinotrophic glucagon-like peptide-2
        analogs)
IT
     Antiulcer agents
       Celiac disease
     Drug delivery systems
     Protein sequences
     Ulcer
        (intestinotrophic glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (malabsorption; intestinotrophic glucagon-like peptide-2
        analogs)
IT
     Intestine, disease
        (short bowel syndrome; intestinotrophic
        glucagon-like peptide-2 analogs)
ΙT
     Intestine, disease
        (small; intestinotrophic glucagon-like peptide-2 analogs)
IT
     Digestive tract
        (sprue; intestinotrophic glucagon-like peptide-2 analogs)
IT
     54249-88-6, Dipeptidyl peptidase IV
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (intestinotrophic glucagon-like peptide-2 analogs)
     89750-15-2D, Glucagon-like peptide 2, analogs
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (intestinotrophic glucagon-like peptide-2 analogs)
IT
     223460-79-5, 1-33-Glucagon-like
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Harle 10 / 042746 Page 25

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325150-33-2
                          325150-06-9
     peptide II (human)
     RL: PRP (Properties)
        (unclaimed protein sequence; intestinotrophic glucagon-like peptide-2
        analogs)
TТ
     81156-22-1
     RL: PRP (Properties)
        (unclaimed sequence; intestinotrophic glucagon-like peptide-2 analogs)
              THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(2) Anon; EP 0612531 1994 HCAPLUS
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    V152(3), P1038 HCAPLUS
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     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (intestinotrophic glucagon-like peptide-2 analogs)
     89750-15-2 HCAPLUS
RN
     Glucagon-like peptide II (9CI) (CA INDEX NAME)
CN
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AN
DN
     132:59448
     Entered STN: 06 Dec 1999
ED
     Glucagon-like peptide 2 decreases mortality and reduces the severity of
TΙ
     indomethacin-induced murine enteritis
     Boushey, Robin P.; Yusta, Bernardo; Drucker, Daniel J.
ΑU
     Department of Medicine, Banting and Best Diabetes Centre, The Toronto
CS
     General Hospital, University of Toronto, Toronto, ON, M5G2C4, Can.
     American Journal of Physiology (1999), 277(5, Pt. 1), E937-E947
SO
     CODEN: AJPHAP; ISSN: 0002-9513
PΒ
     American Physiological Society
\mathsf{DT}
     Journal
LA
     English
     2-6 (Mammalian Hormones)
CC
     Glucagon-like peptides (GLPs) are secreted from enteroendocrine cells in
AB
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Page 26

the gastrointestinal tract. GLP-1 actions regulate blood glucose, whereas GLP-2 exerts trophic effects on intestinal mucosal epithelium. Although GLP-1 actions are preserved in diseases such as diabetes, GLP-2 action has not been extensively studied in the setting of intestinal disease. We have now evaluated the biol. effects of a human GLP-2 analog in the setting of exptl. murine nonsteroidal antiinflammatory drug-induced enteritis. Human (h) [Gly2] GLP-2 significantly improved survival whether administered before, concomitant with, or after indomethacin. The h[Gly2]GLP-2-treated mice exhibited reduced histol. evidence of disease activity, fewer intestinal ulcerations, and decreased myeloperoxidase activity in the small bowel (vs. saline-treated controls). The h[Gly2]GLP-2 significantly reduced cytokine induction, bacteremia, and the percentage of pos. splenic and hepatic bacterial cultures. The h[Gly2]GLP-2 enhanced epithelial proliferation (for increased crypt cell proliferation in h[Gly2]GLP-2- vs. saline-treated mice after indomethacin) and reduced apoptosis in the crypt compartment. These observations demonstrate that a human GLP-2 analog exerts multiple complementary actions that serve to preserve the integrity of the mucosal epithelium in exptl. gastrointestinal injury in vivo. glucagon like peptide 2 indomethacin enteritis

ST

Intestine, disease

(enteritis; glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT Apoptosis

Bacteremia

Cell proliferation

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT Intestine

> (small; glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

53-86-1, Indomethacin

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

TT 197922-42-2, Glucagon-like peptide

II [2-glycine] (human)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

9003-99-0, Myeloperoxidase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

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(46) Yamada, T; Inflammation 1993, V17, P641 HCAPLUS
        197922-42-2, Glucagon-like peptide
TТ
         II [2-glycine] (human)
         RL: BAC (Biological activity or effector, except adverse); BSU (Biological
         study, unclassified); THU (Therapeutic use); BIOL (Biological
         study); USES (Uses)
              (glucagon-like peptide 2 decreases mortality and reduces severity of
              indomethacin-induced murine enteritis)
RN
         197922-42-2 HCAPLUS
        L-Aspartic acid, L-histidylglycyl-L-\alpha-aspartylglycyl-L-seryl-L-
CN
         phenylalanyl-L-seryl-L-\alpha-aspartyl-L-\alpha-glutamyl-L-methionyl-L-
         asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L-\alpha-aspartyl-L-
         asparaginy 1-L-leucy 1-L-alany 1-L-alany 1-L-arginy 1-L-\alpha-asparty 1-L-alany 1-L-arginy 1-L-\alpha-asparty 1-L-alany 1-L-arginy 1-L-alany 1-L-arginy 1-L-alany 1-L-alany 1-L-arginy 1-L-alany 1-L-alany 1-L-alany 1-L-alany 1-L-arginy 1-L-alany 1-L-alany
         phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-
         glutaminyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX
         NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
L50 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
         1999:736497 HCAPLUS
DN
         131:318292
ED
         Entered STN: 19 Nov 1999
        Glucagon-related peptides and their use for the prevention or treatment of
TI
         disorders involving the large intestine
IN
        Drucker, Daniel J.
PA
         1149336 Ontario Inc., Can.
SO
         PCT Int. Appl., 40 pp.
         CODEN: PIXXD2
דת
         Patent
LΑ
         English
IC
         A61K038-26; G01N038-26
        2-6 (Mammalian Hormones)
CC
FAN.CNT 1
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                                                                             APPLICATION NO.
                                                                                                                     DATE
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                                                       19991118 WO 1998-CA477
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                                                                                                                     19980511
               W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
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             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
     AU 9874215
                          A1 19991129
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PRAI WO 1998-CA477
                                 19980511
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CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
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                        A61K038-26IC
                 IC
WO 9958144
                                          G01N038-26
WO 9958144
                 ECLA A61K038/26
    The invention relates to glucagon-related peptides and their use for the
     prevention or treatment of disorders involving the large intestine. In
     particular, it has now been demonstrated that GLP-2 and peptidic agonists
     of GLP-2 can cause proliferation of the tissue of large intestine. Thus,
     the invention provides methods of proliferating the large intestine in a
     subject in need thereof. Further, the methods of the invention are useful
     to treat or prevent inflammatory conditions of the large intestine,
     including inflammatory bowel diseases.
     glucagon like peptide 2 analog large intestine function treatment;
ST
     inflammation intestine treatment GLP2 analog
IT
     Intestine, disease
        (Crohn's; glucagon-related peptides and use for prevention or treatment
        of disorders involving the large intestine)
TT
     Gastrointestinal hormone receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (GLP-2 receptors, agonists; glucagon-related peptides and use for
        prevention or treatment of disorders involving the large intestine)
IT
     Intestine, disease
        (colitis, infections, ischemic, drug-induce colitis
        , or chemical-induced colitis; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)
IT
     Intestine, disease
        (colitis; glucagon-related peptides and use for prevention or
        treatment of disorders involving the large intestine)
IT
     Intestine, disease
        (diverticulitis; glucagon-related peptides and use for
        prevention or treatment of disorders involving the large intestine)
IT
     Anti-inflammatory agents
        (glucagon-related peptides and use for prevention or treatment of
        disorders involving the large intestine)
IT
     Intestine, disease
        (inflammatory; glucagon-related peptides and use for
        prevention or treatment of disorders involving the large intestine)
IT
     Intestine
        (large; glucagon-related peptides and use for enhancing functioning of
        the large intestine by causing proliferation)
IT
     Intestine
        (resection; glucagon-related peptides and use for prevention or
        treatment of disorders involving the large intestine)
IT
     Intestine, disease
        (ulcerative colitis; glucagon-related peptides and
        use for prevention or treatment of disorders involving the large
        intestine)
     89750-15-2, Glucagon like peptide-2 195262-56-7
IT
     195262-56-7D, analogs 197664-29-2 197922-42-2
     197922-60-4 197923-49-2 223460-79-5, 1-33-
     Glucagon-like peptide II (human)
     223460-79-5D, 1-33-Glucagon-like
     peptide II (human), analogs
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (glucagon-related peptides and use for prevention or treatment of
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disorders involving the large intestine)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
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   Physiology 1997, V273(6), PG1252 HCAPLUS
(2) Ontario Inc; WO 9739031 A 1997 HCAPLUS
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(4) Tsai, C; American Journal of Physiology: Endocrinology and Metabolism 1997,
   V273(1), PE77 HCAPLUS
   89750-15-2, Glucagon like peptide-2
IT
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); THU (Therapeutic use); BIOL (Biological
    study); USES (Uses)
       (glucagon-related peptides and use for prevention or treatment of
       disorders involving the large intestine)
RN
    89750-15-2 HCAPLUS
    Glucagon-like peptide II (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
L50 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
    1999:407767 HCAPLUS
AN
DN
    131:28314
ED
    Entered STN: 02 Jul 1999
TI
    Methods of enhancing functioning of the large intestine with
    glucagon-related peptides
IN
   Drucker, Daniel J.
PA
   1149336 Ontario Inc., Can.
   Can. Pat. Appl., 36 pp.
SO
    CODEN: CPXXEB
DT
   Patent
LA
   English
IC
   ICM A61K038-26
    ICS C12Q001-00; G01N033-483
    2-6 (Mammalian Hormones)
FAN.CNT 2
   PATENT NO.
                      KIND DATE
                                       APPLICATION NO.
                                                              DATE
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                                                               _____
                                         ______
PI CA 2236519
                       AA
                             19981102 CA 1998-2236519 19980504
PRAI US 1997-850664
                       A
                             19970502
CLASS
            CLASS PATENT FAMILY CLASSIFICATION CODES
PATENT NO.
 ______
CA 2236519 ICM A61K038-26
               ICS
                      C12Q001-00; G01N033-483
    The invention relates to glucagon-related peptides and their use for the
    prevention or treatment of disorders involving the large intestine. In
    particular, it has now been demonstrated that GLP-2 and peptidic agonists
    of GLP-2 can cause proliferation of the tissue of large intestine. Thus,
    the invention provides methods of proliferating the large intestine in a
    subject in need thereof. Further, the methods of the invention are useful
    to treat or prevent inflammatory conditions of the large intestine,
    including inflammatory bowel diseases. Methods for identifying peptides
    useful to treat inflammatory conditions involving the large intestine are
    also claimed.
ST
    GLP2 treatment intestine inflammation
    Intestine, disease
IT
       (Crohn's; GLP-2 and its analogs for the treatment or prevention of
       inflammatory conditions of the large intestine)
TT
    Anti-inflammatory agents
       (GLP-2 and its analogs for the treatment or prevention of inflammatory
       conditions of the large intestine)
    Gastrointestinal hormone receptors
IT
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
       (GLP-2 receptors, agonists; GLP-2 and its analogs for the treatment or
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prevention of inflammatory conditions of the large intestine)

Page 30

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Intestine, disease
IT
        (colitis, ischemic and infectious and drug or chemical induced;
        GLP-2 and its analogs for the treatment or prevention of
        inflammatory conditions of the large intestine)
IT
     Intestine, disease
        (diverticulitis; GLP-2 and its analogs for the treatment or
        prevention of inflammatory conditions of the large intestine)
IT
     Intestine, disease
        (inflammatory; GLP-2 and its analogs for the treatment or
        prevention of inflammatory conditions of the large intestine)
IT
     Intestine
        (large; GLP-2 and its analogs for the treatment or prevention of
        inflammatory conditions of the large intestine)
IT
     Drug screening
        (methods for identifying peptides useful to treat inflammatory
        conditions involving the large intestine)
IT
     Cell proliferation
        (of intestinal tissue; GLP-2 and its analogs for the treatment or
        prevention of inflammatory conditions of the large intestine)
IT
     Intestine
        (resection; GLP-2 and its analogs for the treatment or prevention of
        inflammatory conditions of the large intestine after resection)
     Intestine, disease
        (ulcerative colitis; GLP-2 and its analogs for the
        treatment or prevention of inflammatory conditions of the
        large intestine)
IT
     89750-15-2, Glucagon-like peptide
     II 89750-15-2D, Glucagon-like
     peptide II, analogs 195262-56-7
     197664-29-2 197922-42-2 197922-60-4
     197923-49-2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (GLP-2 and its analogs for the treatment or prevention of inflammatory
        conditions of the large intestine)
ΙT
     54249-88-6, Dipeptidyl peptidase IV
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (GLP-2 and its analogs resistant to cleavage by DPP-IV for the
        treatment or prevention of inflammatory conditions of the large
        intestine)
IT
     89750-15-2, Glucagon-like peptide
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (GLP-2 and its analogs for the treatment or prevention of inflammatory
        conditions of the large intestine)
     89750-15-2 HCAPLUS
RN
CN
     Glucagon-like peptide II (9CI)
                                      (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
L50 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
     1999:73299 HCAPLUS
AN
DN
     130:218560
     Entered STN: 04 Feb 1999
ED
TI
     Human [Gly2]GLP-2 reduces the severity of colonic injury in a murine model
     of experimental colitis
     Drucker, Daniel J.; Yusta, Bernardo; Boushey, Robin P.;
Deforest, Lorraine; Brubaker, Patricia L.
ΑU
     Department of Medicine, Banting and Best Diabetes Centre, Toronto
CS
     Hospital, ON, Can.
so
     American Journal of Physiology (1999), 276(1, Pt. 1), G79-G91
     CODEN: AJPHAP; ISSN: 0002-9513
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American Physiological Society
PB
DT
    Journal
LΑ
     English
     2-6 (Mammalian Hormones)
CC
     The pathol. of Crohn's disease and ulcerative colitis is characterized by
AΒ
     chronic inflammation and destruction of the gastrointestinal epithelium.
     Although suppression of inflammatory mediators remains the principal
     component of current disease therapeutics, strategies for enhancing repair
     and regeneration of the compromised intestinal epithelium have not been
     widely explored. The demonstration that a peptide hormone secreted by the
     intestinal epithelium, qlucagon-like peptide-2 (GLP-2), is a potent
     endogenous stimulator of intestinal epithelial proliferation in the small
     bowel prompted studies of the therapeutic efficacy of GLP-2 in CD1 and
     BALB/c mice with dextran sulfate (DS)-induced colitis. The authors report
     that a human GLP-2 analog (h[Gly2]GLP-2) significantly reverses weight loss,
     reduces interleukin-1 expression, and increases colon length, crypt depth,
     and both mucosal area and integrity in the colon of mice with acute DS
     colitis. The effects of h[Gly2]GLP-2 in the colon are mediated in part
     via enhanced stimulation of mucosal epithelial cell proliferation. These
     observations suggest that exploitation of the normal mechanisms used to
     regulate intestinal proliferation may be a useful adjunct for healing
     mucosal epithelium in the presence of active intestinal inflammation.
ST
     GLP2 ulcerative colitis colon epithelium
IT
     Intestine
        (colon, epithelium; human [Gly2]GLP-2 reduces severity of colonic
        injury in mice with dextran sulfate-induced colitis)
     Intestine, disease
TТ
       Intestine, disease
        (colon, injury; human [Gly2]GLP-2 reduces severity of colonic
        injury in mice with dextran sulfate-induced colitis)
IT
     Cachexia
     Cell proliferation
        (human [Gly2]GLP-2 reduces severity of colonic injury in mice with
        dextran sulfate-induced colitis)
IT
     Interleukin 1
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (human [Gly2]GLP-2 reduces severity of colonic injury in mice with
        dextran sulfate-induced colitis)
     Intestine, disease
IT
        (ulcerative colitis; human [Gly2]GLP-2 reduces
        severity of colonic injury in mice with dextran
        sulfate-induced colitis)
IT
     9042-14-2, Dextran sulfate
     RL: ADV (Adverse effect, including toxicity); BUU (Biological use,
     unclassified); BIOL (Biological study); USES (Uses)
        (human [Gly2]GLP-2 reduces severity of colonic injury in mice with
        dextran sulfate-induced colitis)
TT
     197922-42-2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (human [Gly2]GLP-2 reduces severity of colonic injury in mice with
        dextran sulfate-induced colitis)
RE.CNT
              THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(2) Bennett, C; J Pharmacol Exp Ther 1997, V280, P988 HCAPLUS
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(6) Brubaker, P; Am J Physiol 1997, V272 (Endocrinol Metab 35), PE1050 (7) Brubaker, P; Endocrinology 1997, V138, P4837 HCAPLUS
(8) Campos, R; Endocrinology 1994, V134, P2156 HCAPLUS
(9) Campos, R; Mol Endocrinol 1994, V9, P1656
(10) Chance, W; Am J Physiol 1997, V273 (Gastrointest Liver Physiol 36), PG559
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- (11) Cheeseman, C; Am J Physiol 1996, V271 (Gastrointest Liver Physiol 34), PG477 (12) Cheeseman, C; Am J Physiol 1997, V273 (Regulatory Integrative Comp Physiol 42), PR1965 (13) Chomczynski, P; Anal Chem 1987, V162, P156 HCAPLUS (14) Cooper, H; Lab Invest 1993, V69, P238 HCAPLUS (15) Dieleman, L; Gastroenterology 1994, V107, P1643 HCAPLUS (16) Domek, M: Scand J Gastroenterol 1995, V30, P1089 MEDLINE (17) Drucker, D; Am J Physiol 1997, V273 (Gastrointest Liver Physiol 36), PG1252 (18) Drucker, D; Am J Physiol 1997, V273 (Gastrointest Liver Physiol 36), PG3 (19) Drucker, D; Nat Biotechnol 1997, V15, P673 HCAPLUS (20) Drucker, D; Proc Natl Acad Sci USA 1996, V93, P7911 HCAPLUS (21) Egger, B; Gastroenterology 1997, V113, P825 HCAPLUS (22) Elson, C; Gastroenterology 1995, V109, P1344 MEDLINE (23) Emmrich, J; Lancet 1991, V1, P570 (24) Fuller, P; Gastroenterology 1993, V104, P459 HCAPLUS (25) Gleeson, M; Gut 1971, V12, P773 MEDLINE (26) Hanauer, S; N Engl J Med 1996, V334, P841 MEDLINE (27) Hodin, R; Surgery 1994, V116, P426 MEDLINE (28) Hogaboam, C; J Clin Invest 1997, V100, P2766 HCAPLUS (29) Housley, R; J Clin Invest 1994, V94, P1764 HCAPLUS (30) Koh, T; Gastroenterology 1997, V113, P1015 HCAPLUS (31) Kojouharoff, G; Clin Exp Immunol 1997, V107, P353 HCAPLUS (32) Lee, Y; Endocrinology 1993, V133, P171 HCAPLUS (33) Mashimo, H; Science 1996, V274, P262 HCAPLUS (34) McCall, R; Gastroenterology 1994, V106, P960 HCAPLUS (35) Minocha, A; Dig Dis Sci 1995, V40, P1757 MEDLINE (36) Murthy, S; Inflamm Res 1997, V46, P224 HCAPLUS (37) Ni, J; Gut 1996, V39, P234 HCAPLUS (38) Okayasu, I; Gastroenterology 1990, V98, P694 MEDLINE (39) Olson, A; J Pediatr Gastroenterol Nutr 1995, V21, P410 HCAPLUS (40) Onderdonk, A; Am J Clin Nutr 1979, V32, P258 MEDLINE (41) Rajora, N; Peptides 1997, V18, P381 HCAPLUS (42) Savendahl, L; Endocrinology 1997, V138, P734 MEDLINE (43) Shintani, N; Clin Exp Immunol 1997, V108, P340 HCAPLUS (44) Stack, W; Lancet 1997, V349, P521 HCAPLUS (45) Stevens, F; Gut 1984, V25, P784 MEDLINE (46) Stronkhorst, A; Gut 1997, V40, P320 HCAPLUS (47) Tang-Christensen, M; Am J Physiol 1996, V271(Regulatory Integrative Comp Physiol 40), PR848 (48) Targan, S; N Engl J Med 1997, V337, P1029 HCAPLUS (49) Taylor, R; Exp Clin Endocrinol 1995, V103, P58 HCAPLUS (50) Thompson, J; Gastroenterology 1997, V113, P1402 MEDLINE (51) Tsai, C; Am J Physiol 1997, V273 (Endocrinol Metab 36), PE77
 (52) Tsai, C; Am J Physiol 1997, V272 (Gastrointest Liver Physiol 35), PG662 (53) Turton, M; Nature 1996, V379, P69 HCAPLUS (54) Wang, T; J Clin Invest 1996, V98, P1918 HCAPLUS (55) Yamada, M; Gut 1992, V33, P1521 HCAPLUS (56) Zeeh, J; Gastroenterology 1996, V110, P1077 HCAPLUS 197922-42-2 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis) RN 197922-42-2 HCAPLUS
- CN L-Aspartic acid, L-histidylglycyl-L-α-aspartylglycyl-L-seryl-Lphenylalanyl-L-seryl-L-α-aspartyl-L-α-glutamyl-L-methionyl-Lasparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L-α-aspartyl-Lasparaginyl-L-leucyl-L-alanyl-L-arginyl-L-α-aspartyl-Lphenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-Lglutaminyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX
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- *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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L50 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
    1998:789042 HCAPLUS
    130:43339
    Entered STN: 16 Dec 1998
ED
TI
    Glucagon-like peptide 2 formulations for enhancing functioning of the
    upper gastrointestinal tract
IN
    Drucker, Daniel J.
PA
    1149336 Ontario Inc., Can.
    PCT Int. Appl., 64 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
    ICM A61K038-26
IC
    ICS A61K038-30; A61K038-27; A61K035-38; G01N033-50; C12N005-06;
         C12N005-08; A61K038-30; A61K038-26; A61K038-27; A61K038-26;
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     63-6 (Pharmaceuticals)
    Section cross-reference(s): 2
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CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
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 WO 9852600
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                       A61K038-26
                       A61K038-30; A61K038-27; A61K035-38; G01N033-50;
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                       C12N005-06; C12N005-08; A61K038-30; A61K038-26;
                       A61K038-27; A61K038-26; A61K038-26; A61K038-18
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                       A61K038/26; A61K038/26+M; A61K038/27+M; A61K038/30+M
                       514/012.000; 435/366.000; 530/308.000; 530/324.000
 US 6051557
                NCL
                       A61K038/26; A61K038/26+M; A61K038/27+M; A61K038/30+M
                ECLA
     The invention relates to glucagon-related peptides and their use for the
AB
     prevention or treatment of disorders involving the upper gastrointestinal
     tract including the esophagus and stomach. In particular, it has now been
     demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause
     proliferation of the tissue of the upper gastrointestinal tract. Thus,
     the invention provides methods of proliferating the upper gastrointestinal
     tract in a subject in need thereof. Further, the methods of the invention
     are useful to treat or prevent inflammatory conditions of the upper
     gastrointestinal tract, including inflammatory diseases. GLP-2 stimulates
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the growth of upper gastrointestinal tissue when administered in conjunction with other peptide hormones. The invention further provides pharmaceutical compns. of GLP-2 with at least one other peptide hormone, methods of enhancing the growth of upper gastrointestinal tissue and of gastrointestinal disorders by increasing serum levels of GLP-2 and at least one other peptide hormone, and kits for performing the methods of the invention.

ST glucagon like peptide 2 upper gastrointestinal tract

IT Intestine, disease

(Crohn's; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (GLP-2 analogs; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (GLP-2, agonists; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Esophagus

(acid reflux; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Stomach, disease

(atrophic gastritis, metaplastic; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Stomach

(bile reflux; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Sarcoidosis

(esophageal; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Esophagus

(esophagitis; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Stomach, disease

(gastritis; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Radiotherapy

(gastrointestinal injury from; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Anti-inflammatory agents

Behcet's syndrome

Esophagus

Genetic engineering Helicobacter pylori

Stomach

(glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Hepatocyte growth factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Transplant and Transplantation

(graft-vs.-host reaction; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Drug delivery systems

(injections, i.v.; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Drug delivery systems

(injections, s.c.; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

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TT
     Drug delivery systems
        (oral; glucagon-like peptide 2 formulations for enhancing functioning
        of the upper gastrointestinal tract)
ΙT
     Surgery
        (resection, of upper gastrointestinal tract; glucagon-like peptide 2
        formulations for enhancing functioning of the upper gastrointestinal
IT
     Cell proliferation
        (stimulation of; glucagon-like peptide 2 formulations for enhancing
        functioning of the upper gastrointestinal tract)
     Digestive tract
        (upper; glucagon-like peptide 2 formulations for enhancing functioning
        of the upper gastrointestinal tract)
IT
     9002-72-6, Somatotropin 9002-72-6D, Somatotropin, analogs
             67763-97-7, Igf-2 148348-15-6, Fibroblast growth factor 7
     Iaf-1
     197922-42-2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PEP (Physical, engineering or chemical process);
     THU (Therapeutic use); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (glucagon-like peptide 2 formulations for enhancing functioning of the
        upper gastrointestinal tract)
TT
     89750-15-2, Glucagon-like peptide 2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PEP (Physical, engineering or chemical process);
     THU (Therapeutic use); BIOL (Biological study); PROC (Process);
     USES (Uses)
        (receptors, agonists; glucagon-like peptide 2 formulations for
        enhancing functioning of the upper gastrointestinal tract)
              THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE CNT
(1) Amgen Inc; WO 9824813 A 1998 HCAPLUS
(2) Drucker, D; American Journal of Physiology: Gastrointestinal and Liver
    Physiology 1997, V273(6, Part 1), PG1252
(3) Drucker, D; Proceedings of the National Academy of Sciences of USA 1996,
    V93, P7911 HCAPLUS
(4) Ontario Inc; WO 9632414 A 1996 HCAPLUS
(5) Ontario Inc; WO 9739031 A 1997 HCAPLUS
(6) Ontario Inc; WO 9825644 A 1998 HCAPLUS
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PEP (Physical, engineering or chemical process);
     THU (Therapeutic use); BIOL (Biological study); PROC (Process);
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        (glucagon-like peptide 2 formulations for enhancing functioning of the
        upper gastrointestinal tract)
RN
     197922-42-2 HCAPLUS
     L-Aspartic acid, L-histidylqlycyl-L-α-aspartylqlycyl-L-seryl-L-
CN
     phenylalanyl-L-seryl-L-\alpha-aspartyl-L-\alpha-glutamyl-L-methionyl-L-
     asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L-α-aspartyl-L-
     asparaginyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L-α-aspartyl-L-
     phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-
     glutaminyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX
     NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
L50 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     1998:402335 HCAPLUS
DN
     129:77032
ED
     Entered STN: 01 Jul 1998
TI
     Compositions containing glucagon-related peptides in combination with
     other agents for enhancing intestinal function
IN
    Drucker, Daniel J.
     1149336 Ontario Inc., Can.; Drucker, Daniel J.
PA
SO
     PCT Int. Appl., 44 pp.
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CODEN: PIXXD2
DT
     Patent
LΑ
     English
     ICM A61K038-30
TC
         A61K038-27; A61K038-26; C12N005-06; C12N005-08; A61K038-30;
          A61K038-26; A61K038-27; A61K038-26; A61K038-26; A61K038-05
     2-6 (Mammalian Hormones)
CC
     Section cross-reference(s): 63
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                                           APPLICATION NO.
                                                                  DATE
     PATENT NO.
                               DATE
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                                19980618 WO 1997-CA945
                                                                   19971210
PΙ
    WO 9825644
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             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
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     US 5952301
                                19990914
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                                                                   19961210
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                                20041109
                        A1
                                19980703
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    AU 9852200
    EP 944396
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                               19990929
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PRAI US 1996-763177
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    WO 1997-CA945
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                                19971210
                CLASS PATENT FAMILY CLASSIFICATION CODES
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WO 9825644
                 ICM
                        A61K038-30
                        A61K038-27; A61K038-26; C12N005-06; C12N005-08;
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                        A61K038-30; A61K038-26; A61K038-27; A61K038-26;
                        A61K038-26; A61K038-05
                 ECLA
                       A61K038/26+M; A61K038/27+M; A61K038/30+M
WO 9825644
                        514/012.000; 435/004.000; 435/387.000; 435/406.000;
 US 5952301
                 NCL
                        530/308.000; 530/399.000
                 ECLA
                        A61K038/26+M; A61K038/27+M; A61K038/30+M
     GLP-2 stimulates the growth of both small intestine and large intestine
AB
     tissue when administered in conjunction with other agents. The invention
     provides pharmaceutical compns. of GLP-2 with at least one other agent
     that increase the biol. activity of GLP-2, methods of enhancing the growth
     of both small and large intestine tissue and of ameliorating nutritional
     or gastrointestinal disorders by increasing serum levels of GLP-2 and at
     least one other agent, and kits for performing the methods of the
     invention.
ST
     GLP intestinal function improvement
IΤ
     Blood vessel, disease
       Celiac disease
     Cell proliferation
     Gene therapy
     Malnutrition
        (compns. containing glucagon-related peptides in combination with other
        agents for enhancing intestinal function)
IT
     Lymphatic system
        (disease, obstruction; compns. containing glucagon-related peptides in
        combination with other agents for enhancing intestinal function)
IT
     Digestive tract
     Endocrine system
        (disease; compns. containing glucagon-related peptides in
```

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combination with other agents for enhancing intestinal function)
TT
    Metabolism, animal
        (disorder; compns. containing glucagon-related peptides in combination with
        other agents for enhancing intestinal function)
IT
     Intestine, disease
        (enteritis; compns. containing glucagon-related peptides in
        combination with other agents for enhancing intestinal function)
     Intestine, disease
IT
        (infarction; compns. containing glucagon-related peptides in combination
        with other agents for enhancing intestinal function)
TT
     Intestine, disease
        (inflammatory; compns. containing glucagon-related peptides in
        combination with other agents for enhancing intestinal function)
IT
     Intestine, disease
        (large; compns. containing glucagon-related peptides in combination with
        other agents for enhancing intestinal function)
ΙT
     Intestine, disease
        (malabsorption; compns. containing glucagon-related peptides in
        combination with other agents for enhancing intestinal function)
     Intestine, disease
IT
        (post-infectious villous atrophy; compns. containing glucagon-related
        peptides in combination with other agents for enhancing intestinal
        function)
     Connective tissue
IT
        (scleroderma; compns. containing glucagon-related peptides in combination
        with other agents for enhancing intestinal function)
IT
     Intestine, disease
        (short bowel syndrome; compns. containing
        glucagon-related peptides in combination with other agents for
        enhancing intestinal function)
TТ
     Intestine, disease
       Intestine, disease
        (small; compns. containing glucagon-related peptides in combination with
        other agents for enhancing intestinal function)
     9002-72-6, GH 9002-72-6D, GH, analogs 12629-01-5, Human growth hormone
TT
     67763-96-6, IGF-1 67763-96-6D, IGF-1, analogs 67763-97-7, IGF 2
     67763-97-7D, IGF 2, analogs 89750-15-2, Glucagon-like peptide-2
     89750-15-2D, Glucagon-like peptide 2, analogs 93927-39-0
     , Glucagon-related peptide II
     (rat) 99120-49-7, Glucagon-related
                          133745-65-0 143045-27-6
     peptide II (human)
     197922-63-7
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (compns. containing glucagon-related peptides in combination with other
        agents for enhancing intestinal function)
     54249-88-6, Dipeptidyl peptidase IV
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (inhibitors; compns. containing glucagon-related peptides in combination
        with other agents for enhancing intestinal function)
              THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE

    Brigham And Women's Hospital; US 5288703 A 1993 HCAPLUS
    Brigham And Women's Hospital; WO 9306839 A 1993 HCAPLUS

(3) Drucker, D; AMERICAN JOURNAL OF PHYSIOLOGY: GASTROINTESTINAL AND LIVER
    PHYSIOLOGY 1997, V273 (6 part 1), PG1252
(4) Drucker, D; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1996,
    V93, P7911 HCAPLUS
(5) Kabi Pharmacia Ab; US 5482926 A 1993 HCAPLUS
(6) Kabi Pharmacia Ab; WO 9325227 A 1993 HCAPLUS
(7) Ontario Inc; WO 9632414 A 1996 HCAPLUS
(8) Ontario Inc; WO 9739031 A 1997 HCAPLUS
```

89750-15-2, Glucagon-like peptide-2

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (compns. containing glucagon-related peptides in combination with other
        agents for enhancing intestinal function)
RN
     89750-15-2 HCAPLUS
CN
     Glucagon-like peptide II (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
L50 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
\mathbf{A}\mathbf{N}
     1998:89268 HCAPLUS
     128:154390
DN
ED
     Entered STN: 16 Feb 1998
     Preparation and agonistic and antagonistic activity of glucagon-like
TI
     peptide 2 analogs
IN
     Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith, Martin
PΑ
     1149336 Ontario Inc., Can.; Allelix Biopharmaceuticals Inc.;
     Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith, Martin
SO
     PCT Int. Appl., 40 pp.
     CODEN: PIXXD2
     Patent
DT
LА
     English
     ICM C07K014-605
IC
     ICS A61K038-26; G01N033-68
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1
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     PATENT NO.
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                                 DATE
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     WO 9803547
                         A1 19980129 WO 1997-CA521
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     CA 2260291
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                          A1
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     JP 2000516579
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CLASS
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 WO 9803547
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                 ICS
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                        C07K014/605
 WO 9803547
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                        530/324.000; 435/069.100; 435/071.100; 435/325.000;
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                        530/308.000
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                        514/012.000; 530/308.000; 530/324.000
 US 6489295
                 NCL
                        C07K014/605
                 ECLA
 US 2003109449
                 NCL
                         514/012.000
                 ECLA
                        C07K014/605
     Antagonists of glucagon-like peptide 2, H-His-Ala-Asp-Gly-Ser-Phe-Ser-Asp-
AB
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ST

IT

ΤТ

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TТ

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RE

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RN

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IN

Glucagon-like peptide-2 analogs

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Glu-Met-Asn-Thr-Ile-Leu-Asp-Asn-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Asn-Trp-Leu-
     Ile-Gln-Thr-Lys-Ile-Thr-Asp-Arg-OH (GLP-2), have been identified. Their
     effects on the growth of gastrointestinal tissue are described. Its
     formulation as a pharmaceutical, and its therapeutic and related uses in
     treating bowel tissue, are described. Also described are methods of
     identifying antagonists of glucagon-like peptide 2. Thus, [Glu2]-GLP-2,
     prepared by standard solid-phase methods using Merrifield resin and
     tert-butoxycarbonyl (Boc) protection, showed a 25% decrease in small bowel
     weight in a CD1 mouse assay.
     glucagon like peptide analog antagonist prepn; bowel tissue growth
     inhibitor peptide prepn
     Diarrhea
        (chronic; preparation and agonistic and antagonistic activity of
       glucagon-like peptide 2 analogs)
     Hyperplasia
        (inhibitors; preparation and agonistic and antagonistic activity of
        glucagon-like peptide 2 analogs)
     Intestine, disease
        (irritable bowel syndrome; preparation and
        agonistic and antagonistic activity of glucagon-like peptide 2 analogs)
     Cholera
        (preparation and agonistic and antagonistic activity of glucagon-like
        peptide 2 analogs)
     Growth inhibitors, animal
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (small bowel tissue; preparation and agonistic and antagonistic activity of
        glucagon-like peptide 2 analogs)
     Neoplasm
        (small bowel; preparation and agonistic and antagonistic activity of
        glucagon-like peptide 2 analogs)
     99120-49-7DP, Glucagon-related peptide
     II (human), analogs 197664-36-1P 197922-12-6P
                                                         197922-35-3P
                    202533-93-5P 202533-95-7P 202606-11-9P
     197922-54-6P
                                   202606-15-3P
                    202606-14-2P
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     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation and agonistic and antagonistic activity of glucagon-like
        peptide 2 analogs)
RE.CNT
              THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) 1149336 Ontario Inc; WO 9632414 A 1996 HCAPLUS
(2) Buhl, T; J BIOL CHEM 1988, V263(18), P8621 HCAPLUS
(3) Matsuyama, T; HORUMON TO RINSHO 1988, V36(4), P317 HCAPLUS
(4) Watanabe, N; BIOCHEM BIOPHYS RES COMMUN 1988, V152(3), P1038 HCAPLUS
     99120-49-7DP, Glucagon-related peptide
     II (human), analogs
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
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        peptide 2 analogs)
     99120-49-7 HCAPLUS
     Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
L50 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
     1997:696789 HCAPLUS
     127:327015
     Entered STN: 05 Nov 1997
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Drucker, Daniel J.; Crivici, Anna E.; Sumner-smith, Martin

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PA
     1149336 Ontario Inc., Can.; Allelix Biopharmaceuticals Inc.
SO
     PCT Int. Appl., 38 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM C07K014-605
     ICS A61K038-26; G01N033-68
     2-2 (Mammalian Hormones)
     Section cross-reference(s): 34, 63
FAN.CNT 3
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                        KIND DATE
                                           APPLICATION NO.
                                                                 DATE
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     WO 9739031
                               19971023 WO 1997-CA252
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            ML, MR, NE, SN, TD, TG
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     CA 2251576
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                         A1
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                                                                  20011207
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CLASS
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WO 9739031
                       C07K014-605
                ICS
                       A61K038-26; G01N033-68
                ECLA C07K014/605
WO 9739031
EP 1231219
               ECLA C07K014/605
     Analogs of glucagon-like peptide-2, a product of glucagon gene expression,
     have been identified as intestinal tissue growth factors. Their
     formulation as pharmaceutical and therapeutic use in treating disorders of
     the small bowel are described.
     glucagonlike peptide analog
ST
IT
     Intestine, disease
        (Crohn's; glucagon-like peptide-2 analogs)
TТ
    Digestive tract
        (disease; glucagon-like peptide-2 analogs)
IT
     Digestion, biological
        (disorder; glucagon-like peptide-2 analogs)
IT
        (expression; glucagon-like peptide-2 analogs)
TТ
     Intestine
     Ulcer
        (glucagon-like peptide-2 analogs)
IT
     Immunoglobulins
        (hypogammaglobulinemia; glucagon-like peptide-2 analogs)
IT
     Intestine, disease
```

```
(inflammatory; glucagon-like peptide-2 analogs)
TT
    Growth factors, animal
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (intestinal tissue growth factors; glucagon-like peptide-2 analogs)
TT
     Intestine, disease
        (malabsorption; glucagon-like peptide-2 analogs)
IT
     Intestine, disease
        (short bowel syndrome; glucagon-like
        peptide-2 analogs)
IT
     184378-22-1P 184378-24-3P
                                197664-23-6P
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     197664-37-2P
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        (glucagon-like peptide-2 analogs)
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     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (glucagon-like peptide-2 analogs)
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     L-phenylalanyl-L-seryl-L-\alpha-aspartyl-L-\alpha-glutamyl-L-methionyl-L-
     asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L-α-aspartyl-L-
     asparaginyl-L-leucyl-L-alanyl-L-threonyl-L-arginyl-L-α-aspartyl-L-
     phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-
     glutaminyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX
     NAME)
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L50 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
     1996:756228 HCAPLUS
AN
DN
    126:19330
     Entered STN: 26 Dec 1996
ED
     Preparation of glucagon-like peptide-2 analogs as as gastrointestinal
TI
     tissue growth factors
IN
    Drucker, Daniel J.
PA
     1149336 Ontario Inc., Can.
SO
     PCT Int. Appl., 55 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM C07K014-605
     ICS A61K038-26
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1
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                        A1 19961017 WO 1996-CA232
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CLASS
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WO 9632414
               ICM
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               ICS
                       A61K038-26
                ECLA C07K014/605
WO 9632414
                NCL
                       514/002.000; 514/003.000; 514/012.000; 530/303.000;
US 5990077
                       530/308.000; 530/324.000
                ECLA C07K014/605
     MARPAT 126:19330
OS
    Glucagon-like peptide-2, a product of glucagon gene expression, and
AB
     analogs of glucagon-like peptide-2, have been identified as
     gastrointestinal tissue growth factors. Their effects on the growth of
     small bowel and pancreatic islets are described. Their formulation as a
     pharmaceutical, and their therapeutic use in treating disorders of the
     bowel, are described. Thus, rat glucagon-like peptide-2, prepared by standard
     solid-phase methods using Boc chemical on a 4-methylbenzhydrylamine (MBHA)
     resin, administered for 10 days, stimulated villus elongation in CD1 mice
     small bowel. Proliferation rates in the proximal jejunum of the treated
     mice were increased 124% over control mice.
    glucagon like peptide prepn gastrointestinotrophic; small bowel growth
ST
     glucagon like peptide; pancreatic islet growth glucagon like peptide
ΙT
     Digestive tract
        (disease; preparation of glucagon-like peptide-2 analogs as as
        gastrointestinal tissue growth factors)
IT
     Pancreatic islet of Langerhans
        (preparation of qlucagon-like peptide-2 analogs as as gastrointestinal
        tissue growth factors)
TT
     Intestine
        (small; preparation of glucagon-like peptide-2 analogs as as
        gastrointestinal tissue growth factors)
ΙT
     89750-15-2P, Glucagon-related peptide
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (degu; preparation of glucagon-like peptide-2 analogs as as gastrointestinal
        tissue growth factors)
IT
     93927-39-0P, Glucagon-related peptide
     II (rat) 99120-49-7P, Glucagon-like
     peptide II (human) 107444-51-9P 184378-22-1P
     184378-24-3P 184378-25-4P 184378-26-5P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
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use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of glucagon-like peptide-2 analogs as as gastrointestinal
        tissue growth factors)
     71567-77-6, Glicentin
TT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (rat: preparation of qlucagon-like peptide-2 analogs as as gastrointestinal
        tissue growth factors)
TT
     89750-15-2P, Glucagon-related peptide
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (degu; preparation of glucagon-like peptide-2 analogs as as gastrointestinal
        tissue growth factors)
     89750-15-2 HCAPLUS
RN
     Glucagon-like peptide II (9CI) (CA INDEX NAME)
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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L26 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
     1999:565944 HCAPLUS
AN
     131:189728
DN
ED
     Entered STN: 08 Sep 1999
     GLP-2 derivatives with helix-content exceeding 25 %, forming partially
TΙ
     structured micellar-like aggregates
IN
     Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin;
     Kaarsholm, Niels C.; Olsen, Helle Birk; Thim, Lars; Bjorn, Soren Erik
     Novo Nordisk A/s, Den.
PA
SO
     PCT Int. Appl., 24 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
     ICM A61K058-26
TC
     ICS C07K014-605
CC
     63-6 (Pharmaceuticals)
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                                              WO 1999-DK80
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             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
         TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                 19990915
                                            AU 1999-27128
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     AU 9927128
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                                 20001220
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        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI
                                 20020212
                                              JP 2000-533156
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     JP 2002504527
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                                              US 2001-908534
                                                                       20010718 <--
     US 2002025933
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                                  20020228
     US 2004127418
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PRAI DK 1998-271
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     DK 1996-931
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     US 1997-36226P
                          P
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     US 1997-922200
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     US 1998-85789P
     US 1999-258187
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WO 1999-DK80
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    US 2001-908534
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                       A61K058-26
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 US 2004127418
                NCL
                       514/012.000
                       A61K038/26; A61K038/28+M; C07K014/605
                ECLA
OS
    MARPAT 131:189728
    The present invention relates to a pharmaceutical composition comprising a
AB
    GLP-2 derivative of improved solubility and/or stability, and to a method for
     improving the solubility and/or stability of GLP-2 or a fragment or an analog
     thereof. Lys30 [Ne-[\gamma-glutamyl (N\alpha-tetradecanoyl)]] hGLP-
     2 was prepared from hGLP-2-OH, EDPA, NMP and Myr-Glu(ONSu)-OBu-tert.
    GLP2 deriv pharmaceutical; micelle aggregate GLP2 deriv pharmaceutical
ST
     Intestine, disease
IT
        (Crohn's; GLP-2 derivs. with helix-content exceeding 25% forming
       partially structured micellar-like aggregates)
тт
    Aggregates
     Buffers
       Intestine, disease
       Intestine, neoplasm
     Micelles
     Preservatives
     Surfactants
     Ulcer
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
IT
     Intestine, disease
        (enteritis; GLP-2 derivs. with helix-content exceeding 25%
        forming partially structured micellar-like aggregates)
TΤ
     Intestine, disease
        (ileitis; GLP-2 derivs. with helix-content exceeding 25%
        forming partially structured micellar-like aggregates)
IT
     Intestine, disease
        (inflammatory; GLP-2 derivs. with helix-content exceeding 25%
        forming partially structured micellar-like aggregates)
     56-81-5, 1,2,3-Propanetriol, biological studies 69-65-8, D-Mannitol
IT
     7647-14-5, Sodium chloride, biological studies
                                                     9005-64-5, Tween 20
     9005-65-6, Tween 80 106392-12-5, Poloxamer 188
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
     99120-49-7, Glucagon-like peptide
IT
                204521-61-9
     II (human)
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
IT
     240483-73-2P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
IT
     99120-49-7D, Glucagon-like peptide
     II (human), derivs. 204401-91-2 204401-92-3
     204401-93-4 240484-09-7 240485-39-6 240485-42-1
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (GLP-2 derivs. with helix-content exceeding 25% forming partially
        structured micellar-like aggregates)
     60-12-8, 2-Phenylethanol 71-00-1, Histidine, biological studies
IT
     77-92-9, biological studies 127-09-3, Sodium acetate
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Glycylglycine 7632-05-5, Sodium phosphate
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (buffer; GLP-2 derivs. with helix-content exceeding 25% forming
        partially structured micellar-like aggregates)
     94-26-8, Butylparaben 99-76-3, Methylparaben 100-51-6, Benzyl alcohol,
IT
                        108-39-4, biological studies
                                                         108-95-2, Phenol,
    biological studies
     biological studies
     RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (preservative; GLP-2 derivs. with helix-content exceeding 25% forming
        partially structured micellar-like aggregates)
RE.CNT
             THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
       6
RE
(1) Clodfelter, D; Pharmaceutical Research 1998, V15(2), P254 HCAPLUS
(2) Novo Nordisk A/S; WO 9507931 A1 1995 HCAPLUS
(3) Novo Nordisk A/S; WO 9731943 A1 1997 HCAPLUS
(4) Novo Nordisk A/S; WO 9808872 A1 1998 HCAPLUS
(5) Ontario Inc; WO 9632414 A1 1996 HCAPLUS
(6) Ontario Inc; WO 9739031 A1 1997 HCAPLUS
    99120-49-7, Glucagon-like peptide
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        (GLP-2 derivs. with helix-content exceeding 25% forming partially
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     99120-49-7 HCAPLUS
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     Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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        structured micellar-like aggregates)
RN
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CN
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L26 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     1998:394356 HCAPLUS
    129:62975
DM
ED
    Entered STN: 27 Jun 1998
ΤI
     Use of keratinocyte growth factors and glucagon-like peptide 2 to increase
     proliferation and/or differentiation of epithelial cells of
     gastrointestinal tract
     Farrell, Catherine L.; Li, Yue-Sheng
IN
    Amgen Inc., USA; Farrell, Catherine L.; Li, Yue-Sheng
PA
SO
     PCT Int. Appl., 158 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
    ICM C07K014-00
IC
    ICS C07K014-605; A61K038-18
CC
     1-9 (Pharmacology)
FAN.CNT 1
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                       KIND DATE
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                                                                 DATE
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    WO 9824813
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    ES 2181054
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                       T3 20030216
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                        A 20000228
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PRAI US 1996-32533P
US 1997-62074P
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    WO 1997-US22735
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CLASS
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                ICM
                       C07K014-00
                       C07K014-605; A61K038-18
                ICS
 WO 9824813
                ECLA
                      A61K038/18C; A61K038/26; A61K038/26+M; C07K014/50;
                       C07K014/605
     The combined use of KGF variants and GLP-2 to increase proliferation
AB
     and/or differentiation of epithelial cells of gastrointestinal tract, especially
     to treat chemotherapy-related mucositis, is disclosed. The effects of KGF
     and GLP-2 are synergistic.
     qastrointestinal epithelium growth differentiation KGF GLP2; keratinocyte
     growth factor GLP2 gastrointestinal epithelium; glucagon like peptide 2
     KGF gastrointestine; mucositis chemotherapy KGF GLP2
IT
    Mucous membrane
        (disease, inflammation, treatment of chemotherapy-induced; use of
        keratinocyte growth factors and glucagon-like peptide 2 to increase
        proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
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TT
    Mucous membrane
        (inflammation, treatment of chemotherapy-induced; use of keratinocyte
        growth factors and glucagon-like peptide 2 to increase proliferation
        and/or differentiation of epithelial cells of gastrointestinal tract)
IT
     Cell differentiation
    Cell proliferation
       Digestive tract
     Epithelium
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
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        (amino acid sequence; use of keratinocyte growth factors and
        glucagon-like peptide 2 to increase proliferation and/or
        differentiation of epithelial cells of gastrointestinal tract)
IT
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     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
TT
     99120-49-7, Glucagon-related peptide
                  126469-10-1D, Fibroblast growth factor 7 (human clone
     II (human)
     32/49 protein moiety reduced), variants
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        qastrointestinal tract)
IT
     197922-42-2
     RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
RN
     197922-42-2 HCAPLUS
     L-Aspartic acid, L-histidylglycyl-L-α-aspartylglycyl-L-seryl-L-
CN
     phenylalanyl-L-seryl-L-\alpha-aspartyl-L-\alpha-glutamyl-L-methionyl-L-
     asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L-\alpha-aspartyl-L-
     asparaginyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L-α-aspartyl-L-
     phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-
     qlutaminyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX
     NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
TT
     99120-49-7, Glucagon-related peptide
     II (human)
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (use of keratinocyte growth factors and glucagon-like peptide 2 to
        increase proliferation and/or differentiation of epithelial cells of
        gastrointestinal tract)
RN
     99120-49-7 HCAPLUS
                                             (CA INDEX NAME)
CN
     Glucagon-like peptide II (human) (9CI)
         1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITDR
SEQ
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Search done by Noble Jarrell

L26 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

1998:183942 HCAPLUS

AN

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DN
     128:253800
ED
     Entered STN: 28 Mar 1998
ΤI
     Cloning and therapeutic use of cancer cachectic factor peptides and
     precursors for treatment of cancer and for weight loss
     Din, Nanni; Farrah, Theresa M.; Rasmussen, Poul Baad; Vissing, Henrik;
IN
     Clausen, Jes
DΔ
     Novo Nordisk A/S, Den.
so
     PCT Int. Appl., 56 pp.
     CODEN: PIXXD2
рΤ
     Patent
LΆ
     English
IC
     ICM C07K014-47
     ICS A61K038-17
     3-2 (Biochemical Genetics)
     Section cross-reference(s): 14, 63
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                                  19970909
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                  ICM
                         C07K014-47
                  ICS
                         A61K038-17
                 ECLA C07K014/47
 WO 9811136
     Novel isolated cancer cachectic factor peptides (CCF) and an isolated
AB
     precursor form (preCCF) is provided. The invention further provides DNA
     constructs encoding cancer cachectic factors, and DNA constructs encoding precursors of cancer cachectic factors. The invention further relates to
     recombinant vectors, and recombinant host cells comprising said DNA
     constructs. Furthermore methods of producing said CCF peptides or said
     preCCF polypeptide are provided. In view of cachexia being one of the
     most common adverse effects of malignancy occurring in about one half of
     untreated cancer patients, and thus being responsible for both shorter
     survival times and a decreased response to therapy, there is a need in the
     art for agents that regulates this unwanted loss of tissue. It is and
     object of the present invention to provide such agents. It is a further
     object of the invention to provide medicaments and methods for preventing
     or treating conditions or disorders arising from obesity, NIDDM, or
     Syndrome X. Pharmaceutical compns. containing glucagon-like peptide 1,
     glucagon-like peptide 2, or growth hormone to reduce appetite or induce
     satiety are also claimed.
     cancer cachectic factor peptide sequence cloning; glucagon like peptide
ST
     obesity human; growth hormone obesity human
     Peptides, biological studies
IT
     RL: BAC (Biological activity or effector, except adverse); BPN
     (Biosynthetic preparation); BSU (Biological study, unclassified); PRP
     (Properties); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
         (CCF (cancer cachectic factor); A cDNA and peptide with relation to
         cancer and weight loss)
IT
     Cachexia
         (cancerous, treatment of; cloning and therapeutic use of cancer
        cachectic factor peptides and precursors for treatment of cancer and
        for weight loss)
```

```
IT
     cDNA sequences
        (for cancer cachectic factor precursors and peptides, of human)
IT
     Appetite depressants
        (glucagon-like peptides as; cloning and therapeutic use of cancer
        cachectic factor peptides and precursors for treatment of cancer and
        for weight loss)
TТ
     Diabetes mellitus
        (non-insulin-dependent, treatment of; cloning and therapeutic use of
        cancer cachectic factor peptides and precursors for treatment of cancer
        and for weight loss)
ΙT
     Protein sequences
        (of cancer cachectic factor precursors and peptides, of human)
ΤT
     Disease, animal
        (syndrome X, treatment of; cloning and therapeutic use of cancer
        cachectic factor peptides and precursors for treatment of cancer and
        for weight loss)
IT
     Neoplasm
        (treatment of cachexia associated with; cloning and therapeutic use of
        cancer cachectic factor peptides and precursors for treatment of cancer
        and for weight loss)
IT
     Obesity
        (treatment of; cloning and therapeutic use of cancer cachectic factor
        peptides and precursors for treatment of cancer and for weight loss)
TT
     198424-11-2D, glycosylated derivs.
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (amino acid sequence; cloning and therapeutic use of cancer cachectic
        factor peptides and precursors for treatment of cancer and for weight
        loss)
     205237-50-9
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                                                        205237-51-0D,
TТ
     glycosylated derivs.
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (cloning and therapeutic use of cancer cachectic factor peptides and
        precursors for treatment of cancer and for weight loss)
                                       89750-14-1, Glucagon-related peptide I
IT
     12629-01-5, Human growth hormone
     89750-15-2, Glucagon-like peptide 2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (cloning and therapeutic use of cancer cachectic factor peptides and
        precursors for treatment of cancer and for weight loss)
IT
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     study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (nucleotide sequence; cloning and therapeutic use of cancer cachectic
        factor peptides and precursors for treatment of cancer and for weight
        loss)
              THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
       3
RE
(1) Incyte Pharmaceuticals Inc; WO 9738100 A1 1997 HCAPLUS
(2) Penio, T; Letters to nature 1996, V379, P739
(3) Tisdale, M; US 5219579 A 1993 HCAPLUS
     89750-15-2, Glucagon-like peptide 2
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (cloning and therapeutic use of cancer cachectic factor peptides and
        precursors for treatment of cancer and for weight loss)
RN
     89750-15-2 HCAPLUS
     Glucagon-like peptide II (9CI) (CA INDEX NAME)
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L26 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
     1998:163617 HCAPLUS
DN
     128:230696
ED
     Entered STN: 19 Mar 1998
     Preparation of lipophilic derivatives of human glucagon-like peptide-2
TI
IN
     Knudsen, Liselotte Bjerre; Sorensen, Per Olaf; Nielsen, Per Franklin
     Novo Nordisk A/S, Den.; Knudsen, Liselotte Bjerre; Sorensen, Per Olaf;
PA
     Nielsen, Per Franklin
SO
     PCT Int. Appl., 26 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
IC
     ICM C07K014-605
     ICS A61K038-26
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1, 2
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             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
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                        514/012.000
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     Derivs. of hGLP-2 (H-His-Ala-Asp-Gly-Ser-Phe-Ser-Asp-Glu-Met-Asn-Thr-Ile-
AΒ
     Leu-Asp-Asn-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Asn-Trp-Leu-Ile-Gln-Thr-Lys-Ile-
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Thr-Asp-Arg-OH), where a lipophilic substituent (such as an acyl group of
    a straight-chain or branched fatty acid) is attached to any one amino acid
    residue, are claimed. For example, Lys30 (Ne-tetradecanoyl) hGLP-2
    was synthesized in 47% yield from the reactants hGLP-2 and tetradecanoic
    acid hydroxysuccinimide ester in the presence of N-ethyl-N,N-
    diisopropylamine (EDPA) and N-methyl-2-pyrrolidone (NMP). The titled
    compds. can be used in the treatment of obesity, small bowel syndrome,
    etc. (no data).
ST
    glucagon like peptide lipophilic deriv prepn; hGLP2 Lys30 tetradecanoyl
    prepn
ΤТ
    Peptides, preparation
    RL: BAC (Biological activity or effector, except adverse); BSU (Biological
    study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of lipophilic derivs. of hGLP-2)
    Obesity
IΤ
        (use of lipophilic derivs. of hGLP-2 for treatment of obesity)
    Intestine, disease
  (use of lipophilic derivs. of hGLP-2 for treatment of small bowel
IT
        syndrome)
TT
    99120-49-7DP, Glucagon-related peptide
    II (human), derivs. 204319-62-0DP, 1-30-Glucagon
     -related peptide II (human), derivs.
    204319-64-2DP, 1-31-Glucagon-related
    peptide II (human), derivs. 204401-90-1DP,
     1-32-Glucagon-related peptide II
     (human), derivs. 204401-91-2P 204401-92-3P
     204401-93-4P 204401-94-5P 204401-95-6P
     204401-96-7P 204401-97-8P 204401-98-9P
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     204461-70-1P
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     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
    use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of lipophilic derivs. of hGLP-2)
IT
     69888-86-4 99120-49-7, Glucagon-related
    peptide II (human)
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of lipophilic derivs. of hGLP-2)
RE.CNT
              THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Buckley, D; WO 9111457 A1 1991 HCAPLUS
(2) Chen, V; US 5512549 A 1996 HCAPLUS
(3) Ontario Inc; WO 9632414 A1 1996 HCAPLUS
    99120-49-7DP, Glucagon-related peptide
     II (human), derivs. 204319-62-0DP, 1-30-Glucagon
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     1-32-Glucagon-related peptide II
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     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of lipophilic derivs. of hGLP-2)
     99120-49-7 HCAPLUS
RN
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CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204319-62-0 HCAPLUS

CN 1-30-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 1-C

PAGE 1-D

PAGE 1-E

RN 204319-64-2 HCAPLUS CN 1-31-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

Search done by Noble Jarrell

Absolute stereochemistry.

PAGE 1-A

PAGE 1-C

PAGE 2-B

PAGE 2-D

PAGE 2-E



CN

lysine] - (9CI) (CA INDEX NAME)

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RN
     204401-90-1 HCAPLUS
     1-32-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    204401-91-2 HCAPLUS
RN
    1-33-Glucagon-like peptide II (human), 20-L-lysine- (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    204401-92-3 HCAPLUS
RN
     1-33-Glucagon-like peptide II (human), 20-L-lysine-30-L-arginine- (9CI)
CN
     (CA INDEX NAME)
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RN
     Glucagon-like peptide II (human), 30-L-arginine-34-L-lysine- (9CI) (CA
CN
     INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204401-94-5 HCAPLUS
RN
     Glucagon-like peptide II (human), 30-L-arginine-34a-L-lysine- (9CI) (CA
CN
     INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204401-95-6 HCAPLUS
     Glucagon-like peptide II (human), 20-L-lysine-30-L-arginine-34a-L-arginine-
CN
      (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204401-96-7 HCAPLUS
RN
     Glucagon-like peptide II (human), 34a-L-arginine- (9CI) (CA INDEX NAME)
CN
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    204401-97-8 HCAPLUS
RN
     1-33-Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-
CN
     (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN
     204401-98-9 HCAPLUS
     1-33-Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-
CN
     30-L-arginine- (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204401-99-0 HCAPLUS
RN
     1-33-Glucagon-like peptide II (human), 20-[N6-(19-carboxy-1-oxononadecyl)-
CN
     L-lysine] - (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204402-00-6 HCAPLUS
RN
     Glucagon-like peptide II (human), 30-[N6-(1-oxotetradecyl)-L-lysine]-
CN
     (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204402-01-7 HCAPLUS
RN
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Glucagon-like peptide II (human), 30-L-arginine-34-[N6-(1-oxotetradecyl)-L-

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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN
     204402-02-8 HCAPLUS
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CN
    oxononadecyl)-L-lysine]- (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
   204402-03-9 HCAPLUS
RN
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CN
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
   204402-04-0 HCAPLUS
RN
    Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-30-L-
CN
    arginine-34a-L-arginine- (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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RN
    Glucagon-like peptide II (human), 30-[N6-(1-oxotetradecyl)-L-lysine]-34a-L-
CN
     arginine- (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204402-06-2 HCAPLUS
RN
     1-33-Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-
CN
     30-[N6-(1-oxotetradecyl)-L-lysine]- (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204402-07-3 HCAPLUS
RN
     Glucagon-like peptide II (human), 30-L-arginine-34a-[N6-(19-carboxy-1-
CN
     oxononadecyl)-L-lysine]- (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     204402-08-4 HCAPLUS
RN
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CN
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    204402-09-5 HCAPLUS
ВИ
    Glucagon-like peptide II (human), 30-[N6-(19-carboxy-1-oxononadecyl)-L-
CN
     lysine]-34a-L-arginine- (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
    204402-10-8 HCAPLUS
RN
     1-33-Glucagon-like peptide II (human), 20-[N6-(19-carboxy-1-oxononadecyl)-
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     L-lysine]-30-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]- (9CI) (CA INDEX
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*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT
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     II (human)
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of lipophilic derivs. of hGLP-2)
RN
     99120-49-7 HCAPLUS
     Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)
CN
SEQ
         1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITDR
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L26 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN
    1997:594753 HCAPLUS
     Entered STN: 17 Sep 1997
ED
ΤI
     Use of a pharmaceutical composition comprising an appetite-suppressing
TN
     Thim, Lars; Wulff, Birgitte Schjellerup; Judge, Martin Edward; Madsen, Ole
    Dragsbaek; Holst, Jens Juul
     Novo Nordisk A/S, Den.
PA
SO
     PCT Int. Appl., 33 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
IC
     ICM C07K014-605
     ICS A61K038-26
CC
     2-6 (Mammalian Hormones)
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                                        APPLICATION NO. DATE
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                       KIND DATE
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                       A1 19970904 WO 1997-DK86
                                                               19970227 <--
     WO 9731943
        W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
            DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM,
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                             19990120 EP 1997-905000
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     EP 1997-905000
                       A3 19970227
     WO 1997-DK86
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CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
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               ICM C07K014-605
                ICS A61K038-26
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                ECLA C07K014/605
 EP 1231218
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                      C07K014/605
                                                                          <--
                       514/012.000; 530/308.000; 530/324.000
 US 5912229
                NCL
                       C07K014/605
                ECLA
os
     MARPAT 127:230020
    The present invention relates to use of an appetite-suppressing
AB
```

```
pharmaceutical composition comprising, together with a pharmaceutically
        acceptable excipient or vehicle, an HPLC fraction of a glucagonoma tumor
        extract prepared by acid ethanol extract, gel filtration and preparative HPLC.
        The fraction contains glucagon-like peptide 2 (GLP-2) as a major component
         (more than 40%). In another aspect, the invention relates to use of a
        pharmaceutically composition comprising GLP-2 or a variant or homolog thereof
         for the prophylaxis of diseases or disorders associated with impaired
        appetite regulation. The appetite-suppressing or satiety-inducing agent
        can also be GLP-1.
ST
        appetite suppressing formulation glucagon like peptide
IT
        Pancreatic islet of Langerhans
            Pancreatic islet of Langerhans
              (glucagonoma; pharmaceutical composition comprising
              appetite-suppressing peptides from a tumor extract)
ΙT
        Diabetes mellitus
              (non-insulin-dependent; pharmaceutical composition comprising
              appetite-suppressing peptides)
IT
        Appetite depressants
        Obesity
              (pharmaceutical composition comprising appetite-suppressing peptides)
TΤ
        89750-14-1, Glucagon-related peptide I 89750-15-2, Glucagon-like
        peptide 2 99120-49-7, Glucagon-related
        peptide II (human)
                                            99658-04-5 116111-21-8,
        Glucagon-like peptide II (swine)
                               195262-60-3
        195262-56-7
        RL: BAC (Biological activity or effector, except adverse); BSU (Biological
         study, unclassified); THU (Therapeutic use); BIOL (Biological
        study); USES (Uses)
              (pharmaceutical composition comprising appetite-suppressing peptides)
TΤ
         89750-15-2, Glucagon-like peptide 2 99120-49-7,
        Glucagon-related peptide II (human)
        116111-21-8, Glucagon-like peptide
         II (swine) 195262-56-7
        RL: BAC (Biological activity or effector, except adverse); BSU (Biological
         study, unclassified); THU (Therapeutic use); BIOL (Biological
        study); USES (Uses)
              (pharmaceutical composition comprising appetite-suppressing peptides)
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         89750-15-2 HCAPLUS
CN
        Glucagon-like peptide II (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
        99120-49-7 HCAPLUS
RN
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                                                                              (CA INDEX NAME)
CN
SEQ
                1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITDR
RN
         116111-21-8 HCAPLUS
CN
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SEQ
                1 HADGSFSDEM NTVLDNLATR DFINWLLHTK ITD
         195262-56-7 HCAPLUS
RN
CN
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        phenylalanyl-L-seryl-L-\alpha-aspartyl-L-\alpha-glutamyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-methionyl-L-met
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         asparaginyl-L-leucyl-L-alanyl-L-threonyl-L-arginyl-L-α-aspartyl-L-
        phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-
        glutaminyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX
        NAME)
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SEQ

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Copyright (c) 2005 Elsevier B.V. All rights reserved.

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- L44 ANSWER 1 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
- AN 2005384300 EMBASE

substance identification.

- TI Teduglutide (ALX-0600), a dipeptidyl peptidase IV resistant qlucagon-like peptide 2 analogue, improves intestinal function in short bowel syndrome patients.
- AU Jeppesen P.B.; Sanguinetti E.L.; Buchman A.; Howard L.; Scolapio J.S.; Ziegler T.R.; Gregory J.; Tappenden K.A.; Holst J.; Mortensen P.B.
- CS Dr. P.B. Jeppesen, Department of Medicine CA-2121, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark. Bekker@dadlnet.dk
- SO Gut, (2005) Vol. 54, No. 9, pp. 1224-1231.

Refs: 24

ISSN: 0017-5749 CODEN: GUTTAK

- CY United Kingdom
- DT Journal; Article
- FS 030 Pharmacology
 - 037 Drug Literature Index
 - 038 Adverse Reactions Titles
 - 048 Gastroenterology
- LA English
- SL English
- ED Entered STN: 20050922
 - Last Updated on STN: 20050922
- Background and aims: Glucagon-like peptide 2 (GLP-2) may improve AB intestinal absorption in short bowel syndrome (SBS) patients with an end jejunostomy. Teduglutide (ALX-0600), a dipeptidyl peptidase IV resistant GLP-2 analogue, prolongs the intestinotrophic properties of GLP-2 in animal models. The safety and effect of teduglutide were investigated in SBS patients with and without a colon in continuity. Methods: Teduglutide was given subcutaneously for 21 days once or twice daily to 16 SBS patients in the per protocol investigational group, 10 with end jejunostomy (doses of 0.03 (n = 2), 0.10 (n = 5), or 0.15 (n = 3) mg/kg/day), one with <50% colon in continuity (dose 0.03 mg/kg/day), and five with ≥ 50% colon in continuity (dose 0.10 mg/kg/day). Nutrient balance studies, D-xylose tests, and intestinal mucosa biopsies were performed at baseline, on the last three days of treatment, and after three weeks of follow up. Pre-study fasting native GLP-2 levels were determined for the five patients with \geq 50% colon in continuity. Results: Pooled across groups and compared with baseline, teduglutide increased absolute (+743 (477) g/day; p<0.001) and relative (+22 (16)%; p<0.001) wet weight absorption, urine weight (+555 (485) g/day; p<0.001), and urine sodium excretion (+53 (40) mmol/day; p<0.001). Teduglutide decreased faecal wet weight (-711 (734) g/day; p = 0.001) and faecal energy excretion (-808 (1453) kJ/day (-193 (347) kcal/day); p = 0.040). In SBS patients with end jejunostomy, teduglutide significantly increased villus height (+38 (45)%; p = 0.030), crypt depth (+22 (18)%; p = 0.010),

and mitotic index (+115 (108)%; p = 0.010). Crypt depth and mitotic index did not change in colonic biopsies from SBS patients with colon in continuity. The most common side effects were enlargement of the stoma nipple and mild lower leg oedema. The improvements in intestinal absorption and decreases in faecal excretion noted after treatment had reversed after the drug free follow up period. A controlled study with a more robust design is ongoing in order to determine the optimal dosage of teduglutide for SBS patients to achieve the maximal effect and utility of this drug in clinical practice. Conclusion: Teduglutide, at three dose levels for 21 days, was safe and well tolerated, intestinotrophic, and significantly increased intestinal wet weight absorption in SBS patients with an end jejunostomy or a colon in continuity. Medical Descriptors: *short bowel syndrome: DT, drug therapy stoma leg edema: SI, side effect intestine absorption sodium urine level sodium excretion feces jejunostomy intestine mucosa biopsy intestine villus crypt cell mitosis index drug safety drug tolerability injection site reaction: SI, side effect headache: SI, side effect abdominal pain: SI, side effect erythema: SI, side effect rash: SI, side effect skin induration: SI, side effect skin bruising: SI, side effect drug effect dehydration: SI, side effect sepsis: SI, side effect infection: SI, side effect human male female clinical article controlled study aged adult article priority journal Drug Descriptors: *teduglutide: AE, adverse drug reaction *teduglutide: DT, drug therapy *teduglutide: PD, pharmacology *teduglutide: SC, subcutaneous drug administration *glucagon like peptide 2: AE, adverse drug reaction *glucagon like peptide 2: DT, drug therapy *glucagon like peptide 2: PD, pharmacology
*glucagon like peptide 2: SC, subcutaneous drug administration unclassified drug (teduglutide) 287714-30-1 Alx 0600 L44 ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN 2005369960 EMBASE

Treatment of gastrointestinal disorders: Teduglutide.

RN

CN

TT ΑU

Mealy N.E.; Bayes M.

```
N.E. Mealy, Prous Science, P.O. Box 540, 08080 Barcelona, Spain
CS
     Drugs of the Future, (2005) Vol. 30, No. 6, pp. 649.
SO
     ISSN: 0377-8282 CODEN: DRFUD4
CY
     Spain
DT
     Journal; Note
FS
     037
             Drug Literature Index
     048
             Gastroenterology
LΑ
     English
     Entered STN: 20050929
ED
     Last Updated on STN: 20050929
     Medical Descriptors:
CT
     Crohn disease: DT, drug therapy
     short bowel syndrome: DT, drug therapy
     drug synthesis
     drug marketing
     human
     clinical trial
     note
     Drug Descriptors:
     *teduglutide: CT, clinical trial
*teduglutide: DT, drug therapy
     *glucagon like peptide 2: CT, clinical trial
     *glucagon like peptide 2: PD, pharmacology
     unclassified drug
RN
     (teduglutide) 287714-30-1
     NPS Pharmaceuticals; Technology Partnership Canada
CO
     ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights
L44
     reserved on STN
ΑN
     2005124077 EMBASE
     Glucagon-like peptide 2: An update.
TI
ΑU
     Shin E.D.; Drucker D.J.; Brubaker P.L.
     P.L. Brubaker, Medical Sciences Building, University of Toronto, 1 King's
CS
     College Circle, Toronto, Ont. M5S 1A8, Canada. p.brubaker@utoronto.ca
     Current Opinion in Endocrinology and Diabetes, (2005) Vol. 12, No. 1, pp.
SO
     63-71.
     Refs: 126
     ISSN: 1068-3097 CODEN: CENDES
CY
     United States
     Journal; General Review
DT
FS
             Endocrinology
     030
             Pharmacology
             Drug Literature Index
     037
LΑ
     English
SL
     English
ED
     Entered STN: 20050331
     Last Updated on STN: 20050331
     Purpose of review: Glucagon-like peptide 2 (GLP-2) is a 33-amino acid
AΒ
     peptide secreted in a nutrient-dependent manner from gut enteroendocrine
     cells. The proliferative and antiapoptotic actions of GLP-2 lead to
     expansion of the mucosal surface area and enhanced capacity for nutrient
     absorption in multiple models of experimental intestinal injury. These
     findings have raised the possibility that GLP-2 administration may produce
     therapeutic benefit in humans with intestinal insufficiency. Recent
     findings: The actions of GLP-2 appear restricted to the gastrointestinal
     tract, central nervous system, and skeleton. GLP-2 exerts its effects
     through a G-protein-coupled receptor expressed in enteric neurons or
     enteroendocrine cells, suggesting that many of its actions are likely
     indirect through as yet unidentified secondary mediators. Exogenous
     administration of GLP-2 to mice, rats, or pigs reduces morbidity
     associated with intestinal damage and improves the structure and function
     of the intestinal mucosal. GLP-2 also exerts anabolic actions in bone via
     prevention of resorption. GLP-2 may also act in the brain to enhance
     neuronal survival via direct antiapoptotic actions. The cytoprotective
     and proliferative actions of GLP-2 highlight the need for further
```

information on the efficacy and safety of long-term administration of GLP-2 in human subjects. Summary: The available evidence suggests that GLP-2 upregulates pathways promoting restoration of intestinal barrier and absorptive function, leading to reduced bacterial translocation, improved nutrient uptake, and enhanced energy absorption. Degradation-resistant GLP-2 analogues are currently being tested in human clinical trials of subjects with inflammatory bowel disease and short bowel syndrome. Hence, GLP-2 may ultimately be used as a therapeutic agent for the treatment of metabolic disorders characterized by insufficient nutrient absorption. .COPYRGT. 2005 Lippincott Williams & Wilkins.

CT Medical Descriptors: *hormone action

intestine injury gastrointestinal tract central nervous system

skeleton

intestine mucosa

osteolysis

cell protection

intestine absorption

bacterial translocation

energy absorption

enteritis

short bowel syndrome

metabolic disorder

drug mechanism

human

nonhuman

review

Drug Descriptors:

*glucagon like peptide 2: PD, pharmacology

*teduglutide: PD, pharmacology

G protein coupled receptor

unclassified drug

RN (teduglutide) 287714-30-1

CN (1) Teduglutide

CO (1) NPS Pharmaceuticals

=> b biosis

FILE 'BIOSIS' ENTERED AT 09:26:12 ON 17 OCT 2005

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FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 October 2005 (20051012/ED)

FILE RELOADED: 19 October 2003.

=> d all 149 tot

- L49 ANSWER 1 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
- AN 2005:59078 BIOSIS
- DN PREV200500059002
- TI Growth factors and trefoil peptides in gastrointestinal health and disease.
- AU Playford, Raymond J. [Reprint Author]; Ghosh, Subrata; Mahmood, Asif
- CS Hammersmith HospFac MedDept Gastroenterol, Univ London Imperial Coll Sci Technol and Med, Du Cane Rd, London, W12 ONN, UK r.playford@imperial.ac.uk
- SO Current Opinion in Pharmacology, (December 2004) Vol. 4, No. 6, pp. 567-571. print.
 ISSN: 1471-4892 (ISSN print).
- DT Article

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General Review; (Literature Review)
T.A
     English
ED
     Entered STN: 3 Feb 2005
     Last Updated on STN: 3 Feb 2005
     Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids
CC
                                                                  10064
     Digestive system - Physiology and biochemistry
     Digestive system - Pathology
                                    14006
     Endocrine - Pituitary
                             17014
     Neoplasms - Pathology, clinical aspects and systemic effects
                                                                     24004
     Immunology - General and methods
                                        34502
ΙT
     Major Concepts
        Biochemistry and Molecular Biophysics; Digestive System (Ingestion and
        Assimilation)
IT
     Diseases
        colon carcinoma: digestive system disease, neoplastic disease
        Colonic Neoplasms (MeSH); Carcinoma (MeSH)
IT
          gastrointestinal disease: digestive system disease
          Gastrointestinal Diseases (MeSH)
IT
     Diseases
        inflammatory bowel disease: digestive system disease
        Inflammatory Bowel Diseases (MeSH)
IT
     Diseases
        short bowel syndrome: digestive system disease
        Short Bowel Syndrome (MeSH)
IT
     Chemicals & Biochemicals
        epidermal growth factor; glucagon-like peptide 2; growth factors;
        growth hormone; monoclonal antibody: production; trefoil peptides
IT
     Miscellaneous Descriptors
        gastrointestinal health status
RN
     62229-50-9 (epidermal growth factor)
       89750-15-2 (glucagon-like peptide 2)
     9002-72-6 (growth hormone)
L49 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN
     2004:42129 BIOSIS
DN
     PREV200400043427
TI
     Dual regulation of cell proliferation and survival via activation of
     glucagon-like peptide-2 receptor signaling.
     Estall, Jennifer L.; Drucker, Daniel J. [Reprint Author]
ΔIJ
     Department of Laboratory Medicine and Pathobiology, Banting and Best
CS
     Diabetes Centre, Toronto General Hospital, University of Toronto, Toronto,
     ON, M5G 2C4, Canada
     d.drucker@utoronto.ca
     Journal of Nutrition, (November 2003) Vol. 133, No. 11, pp. 3708-3711.
SO
     print.
     ISSN: 0022-3166 (ISSN print).
DT
     Article
     English
LΆ
ED
     Entered STN: 14 Jan 2004
     Last Updated on STN: 14 Jan 2004
     Peptide hormones regulate cell viability and tissue integrity, directly or
AΒ
     indirectly, through activation of G-protein-coupled receptors via diverse
     mechanisms including stimulation of cell proliferation and inhibition of
     cell death. Glucagon-like peptide-2 (GLP-2) is a 33 amino acid peptide
     hormone released from intestinal endocrine cells following nutrient
     ingestion. GLP-2 stimulates intestinal crypt cell proliferation leading
     to expansion of the gastrointestinal mucosal epithelium. Exogenous GLP-2
     administration attenuates intestinal injury in experimental models of
     gastrointestinal disease and improves intestinal
     absorption and nutritional status in human patients with intestinal
     failure secondary to short bowel syndrome. GLP-2 also promotes mucosal
     integrity via reduction of injury-associated apoptosis in the intestinal
     mucosa and directly reduces apoptosis in cells expressing the GLP-2
     receptor in vitro. Hence, the regenerative and cytoprotective properties
```

of GLP-2 contribute to its therapeutic potential for the treatment of patients with intestinal disease.

Biochemistry studies - General CC 10060

Metabolism - General metabolism and metabolic pathways 13002 Digestive system - Physiology and biochemistry Digestive system - Pathology 14006

Endocrine - General 17002

IT Major Concepts

> Biochemistry and Molecular Biophysics; Clinical Endocrinology (Human Medicine, Medical Sciences); Gastroenterology (Human Medicine, Medical Sciences); Metabolism

Parts, Structures, & Systems of Organisms IT

cell, proliferation, survival; intestinal endocrine cells: digestive system, endocrine system

TΤ Chemicals & Biochemicals

> G-protein-coupled receptor; glucagon-like peptide-2; glucagon-like peptide-2 receptor: signaling

ORGN Classifier

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human (common): patient

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 89750-15-2 (glucagon-like peptide-2)

ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN L49

2003:106962 BIOSIS AN

PREV200300106962 DN

TI Glucagon-liké peptides: Regulators of cell proliferation, differentiation, and apoptosis.

Drucker, Daniel J. [Reprint Author] ΑU

Toronto General Hospital, 200 Elizabeth Street, MBRW4R-402, Toronto, ON, CS M5G 2C4, Canada d.drucker@utoronto.ca

Molecular Endocrinology, (February 2003) Vol. 17, No. 2, pp. 161-171. SO print.

ISSN: 0888-8809 (ISSN print).

DT Article

General Review; (Literature Review)

LΑ

ED Entered STN: 26 Feb 2003

Last Updated on STN: 26 Feb 2003

AΒ Peptide hormones are secreted from endocrine cells and neurons and exert their actions through activation of G protein-coupled receptors to regulate a diverse number of physiological systems including control of energy homeostasis, gastrointestinal motility, neuroendocrine circuits, and hormone secretion. The glucagon-like peptides, GLP-1 and GLP-2 are prototype peptide hormones released from gut endocrine cells in response to nutrient ingestion that regulate not only energy absorption and disposal, but also cell proliferation and survival. GLP-1 expands islet mass by stimulating pancreatic beta-cell proliferation and induction of islet neogenesis. GLP-1 also promotes cell differentiation, from exocrine cells or immature islet progenitors, toward a more differentiated beta-cell phenotype. GLP-2 stimulates cell proliferation in the gastrointestinal mucosa, leading to expansion of the normal mucosal epithelium, or attenuation of intestinal injury in experimental models of intestinal disease. Both GLP-1 and GLP-2 exert antiapoptotic actions in vivo, resulting in preservation of beta-cell mass and gut epithelium, respectively. Furthermore, GLP-1 and GLP-2 promote direct resistance to apoptosis in cells expressing GLP-1 or GLP-2 receptors. Moreover, an increasing number of structurally related peptide hormones and neuropeptides exert cytoprotective effects through G protein-coupled receptor activation in diverse cell types. Hence, peptide hormones, as exemplified by GLP-1 and GLP-2, may prove to be useful adjunctive tools

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for enhancement of cell differentiation, tissue regeneration, and
     cytoprotection for the treatment of human disease.
CC
     Cytology - Animal
                        02506
     Nutrition - General studies, nutritional status and methods
                                                                    13202
     Digestive system - Physiology and biochemistry 14004
     Digestive system - Pathology
                                    14006
     Endocrine - General
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                           17002
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IT
     Major Concepts
        Digestive System (Ingestion and Assimilation); Endocrine System
        (Chemical Coordination and Homeostasis)
ΙT
     Parts, Structures, & Systems of Organisms
        gut endocrine cell: digestive system, endocrine system; pancreatic
        beta-cell: endocrine system, apoptosis, differentiation, proliferation;
        pancreatic islet: endocrine system
ΙT
     Diseases
        intestinal disease: digestive system disease, etiology
          Gastrointestinal Diseases (MeSH)
ΙT
     Chemicals & Biochemicals
        glucagon-like peptide-1: anti-apoptotic activity, cell regulator,
        prototype peptide hormone; glucagon-like peptide-2: anti-apoptotic
        activity, cell regulator, prototype peptide hormone; nutrient
RN
     89750-14-1 (glucagon-like peptide-1)
       89750-15-2 (glucagon-like peptide-2)
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